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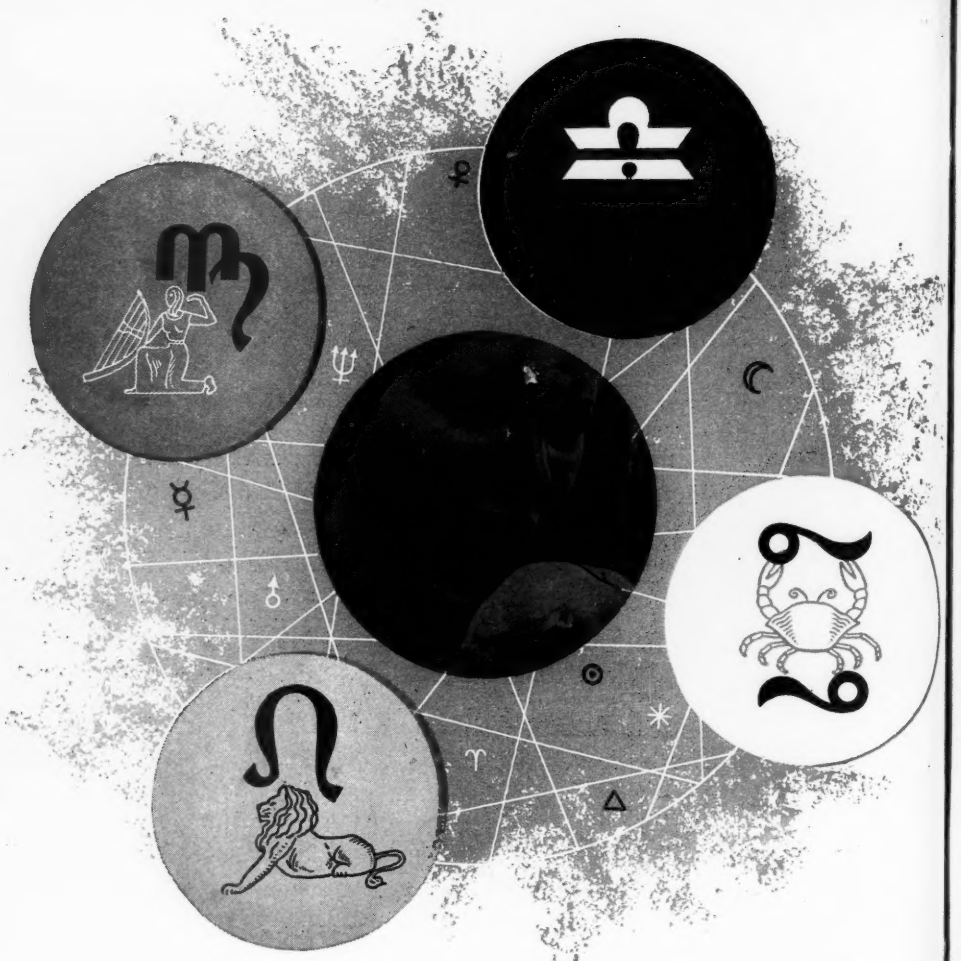

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Volume 247 AUGUST 21, 1952 Number 8

ARTERIAL HYPERTENSION — THE THERAPEUTIC EFFECT OF CATION-EXCHANGE RESINS*

ROBERT J. GILL, M.D.,† AND GARFIELD G. DUNCAN, M.D.‡

With the Technical Assistance of MARTHA A. HUNSCHER, B.S.§

PHILADELPHIA

THE clinical application of cation-exchange resins provides a new means of controlling the sodium content of the body. Several reports on their uses and limitations in edematous states have been published,[1-7] and one favorable report[8] has been issued concerning their use in 6 patients with hypertension during a short-term study.

Cation-exchange-resin therapy for hypertension rests upon three basic premises: these large, organic polymerized molecules are capable of absorbing sodium from ingested food and from the intestinal tract; restriction of the intake of sodium lowers the blood pressure in many patients with hypertension; and the rigid restriction of sodium needed to lower the blood pressure is difficult to attain in homes and restaurants, and even more difficult to maintain over a prolonged period by diet alone because of the unpalatability of such diets.

One might expect that cation-exchange resins would lower the blood pressure of ambulatory patients whose hypertension is sensitive to severe restrictions in dietary sodium, but whose blood pressure had not responded favorably, in general, because of inadequate sodium restriction. Also, resins might intensify the reduction of the blood pressure in patients who had shown a favorable response to moderate restriction of dietary sodium, and finally, the resins might ease the lot of those known sodium-sensitive hypertensive patients by allowing them to have more palatable diets. To test these possibilities, a continuing study of 60 outpatients with essential hypertension was undertaken a year ago at the Pennsylvania Hospital.

This preliminary report on the treatment of hypertension with cation-exchange resins is aimed at clarifying the problems involved in the handling of ambulatory patients taking these substances, to show that sufficient sodium restriction to produce a fall in blood pressure from high to normal levels is safe and feasible in the properly selected patient with the aid of the resins, and to encourage a wider investigation of the resins in the treatment of essential hypertension.

The results are reported on 38 ambulatory patients who have been a part of this study for four to ten months and who have received amounts of dietary sodium varying from 1 to 3 gm. while receiving an ammonium and potassium carboxylic cation-exchange resin, the potassium being added to prevent depletion of body potassium. The ammonium is replaced in the stomach by hydrogen, which in turn is exchanged for sodium in the intestinal tract. In this state the sodium is excreted in the stool. The product used is known commercially as Resodec.¶ A placebo was made by the addition to the resin of the amount of sodium it theoretically will remove in vivo. This resin has an invivo capacity for sodium absorption of 1 or 2 milliequiv. per gram with a daily sodium intake of 1 gm.

Each patient had a diastolic pressure of at least 100 and at least moderately good renal function. No patient was in the malignant phase of hypertension, but all ranged from Groups I to III of the Keith, Wagener and Barker classification,[9] the majority being in Group II. Adequacy of renal function was determined by the urinalysis, dilution concentration test, phenolsulfonphthalein test and blood urea nitrogen determination. In some cases urea clearance tests, intravenous urograms or urine cultures were performed.

Other baseline and follow-up studies included electrocardiogram, funduscopic examination by an ophthalmologist, teleroentgenogram, ballistocardiogram, complete blood count, Sodium Amytal and cold-pressor tests and, as indicated, tests to rule

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Much of the cost of this study was defrayed by Smith, Kline, and French Laboratories, Philadelphia.

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§Director, Food Clinic, Pennsylvania Hospital.

¶Resodec and its placebo were kindly supplied by Smith, Kline and French Laboratories, Philadelphia.

out pheochromocytoma. Each patient had a complete history and physical examination.

During resin therapy, chemical analyses of the blood were done at short intervals, and a quantitative analysis of a twenty-four-hour urine specimen for sodium was done at each visit, the internal standard flame photometer being used. The patients were seen at intervals of one or two weeks by the same physician; the blood pressure was determined each time in the sitting position and on the same arm. Determinations were made at the start of the interview and again after ten or fifteen minutes of relaxation and casual conversation with the physician. The lowest blood pressure of five determinations was recorded.

TABLE 1. *Illustrative Diet Containing Approximately 1 Gm. of Sodium.*

MEAL	HOUSEHOLD MEASURE	SODIUM*
		mg.
Breakfast:		
Eggs	2	81
Cereal cooked without salt	½ cup (20 gm. dry)	Trace
Bread, white, enriched, without salt	2 slices (25 gm. each)	14
Salted butter	1 teaspoon (5 gm.)	49
Fruit, orange juice	½ cup	Trace
Skim milk	8 ounces	125
Noon meal:		
Meat, fish, fowl (fresh)	2-3 ounces (75 gm. as purchased)	55
Milk, skim	8 ounces	125
Fresh vegetables without salt	1 serving	48±
Bread, white, without salt	2 slices (25 gm. each)	14
Salted butter	1 teaspoon	49
Fruit	As desired	—
Evening meal:		
Meat, fish, fowl (fresh)	3-4 ounces (150 gm. as purchased)	110±
Potato, corn or lima beans, fresh	1 serving	—
Fresh vegetables without salt	2 servings	Trace
Bread, without salt	1 slice (25 gm.)	96±
Salted butter	1 teaspoon (5 gm.)	7
Fruit	As desired	49
Total		—
		822 (0.822 gm.)†

*Sodium and potassium in foods according to Bills et al.[10]

†Sodium content is approximate and will vary slightly depending upon choice of meats and vegetables. Potassium content is approximately 3.5 gm., and protein content 92 gm. This diet may be changed to approximately 1.5 gm. of sodium content by the substitution of 4 slices of regular bread for salt-free bread. The 1.5-gm. sodium content may be raised to approximately 2 gm. by addition of 2 slices of bacon. If desired, the dietary sodium increases may be made by the use of salt tablets of known weight, crushed and used as seasoning, rather than by a change in the food content.

Initially a diet containing 1 gm. of sodium was given (Table 1). Diets were prepared using the figures for sodium and potassium contents of various foods as given by Bills.[10] Due allowance was made for racial, religious and personal food preferences. The diets were individually composed and prescribed after interviews with a dietitian and frequent reviews, and desired feasible changes were made throughout the course of the study. This phase of the program was considered to be as important as the drug therapy itself. Resodec was given in doses of 15 gm. three times daily after meals. Calcium lactate, 2 gm., and potassium citrate, 2-3 gm., daily starting about two to four weeks after the onset of therapy were given to prevent calcium and potassium deficiencies and to help minimize the tendency toward hyperchloremic acidosis. Salt substitutes were permitted. Resodec was used for two to five months and then replaced by a placebo — indistinguishable by the patient from the therapeutic Resodec — for periods of six weeks to three months. Some patients were given placebo initially and Resodec subsequently. In some cases 4 gm. of enteric-coated sodium chloride tablets were added to the resin program rather than the substitution of placebo.

CORRELATION OF URINARY SODIUM AND BLOOD-PRESSURE LEVELS

Corcoran, Taylor and Page[11] have shown that significant reductions in blood pressure occur only when the twenty-four-hour urinary sodium is 0.5 gm. or less. They found, as Allen[12] had previously observed, that a lag period of four weeks may precede a lowering of blood pressure after the required level of urinary sodium has been attained. We have found that as long as two months may pass before a lowering of the blood pressure is seen, and we do not consider a patient to be nonsensitive to sodium restriction unless after two months of treatment, during which time the twenty-four-hour urinary sodium is 0.5 gm. or less, the blood pressure is not appreciably lowered. If the urinary sodium does not decrease to these levels it is not known what the status of the patient's hypertension is in regard to sodium sensitivity. Infrequently, the pressures are reduced on a somewhat less rigid restriction of sodium. In view of the fact that the resins divert sodium, but not chloride, from the body, it is necessary to measure urinary excretion of sodium rather than chloride as would suffice when diets low merely in salt content are concerned.

TABLE 2. *Results of Cation-Exchange Resin and Restriction of Dietary Sodium Therapy in Hypertension.*

RESULT	NO. OF CASES
Decrease in diastolic pressure of 20 or more	15 (39%)
Decrease in diastolic pressure to 100 or below	17 (45%)
Combined decrease in diastolic pressure of 20 or more and to 100 or below	9 (24%)
Total	38

RESULTS

Fifteen of the 38 patients had a sustained mean reduction in the diastolic pressure of 20 or more (Table 2); 17 had a mean reduction in the diastolic pressure to 100 or below, and 9 had both a reduction in the diastolic pressure of 20 or greater and a reduction of the diastolic pressure to 100 or below. We consider this combined change to be a good response. In addition, 22 patients had a sustained decrease in systolic pressure of 25 or more.

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Confirming Allen's[12] frequently repeated claims, the greatest lowering of the blood pressure is closely associated with the smallest urinary sodium excretions, especially in cases in which these values are consistently below 0.5 gm. per twenty-four hours (Table 3). However, the hypotensive effect is maintained in some cases in which the excretion of sodium is not consistently below this value. In no case in which the urinary sodium excretions were consistently greater than 0.5 gm. per twenty-four hours was there a good response.

The relations between the prescribed dietary sodium intake and blood-pressure responses are depicted in Table 4. Of the 15 patients having a reduction in the diastolic pressure of 20 or more, 14 had a prescribed intake of 1 to 1.25 gm. of sodium as provided in the diet presented in Table 1. Of the 17 patients with a reduction of the diastolic pressure to less than 100, 12 had a prescribed intake of 1.0 to 1.25 gm. of sodium. Of the 9 patients achieving both a reduction of 20 or better in the diastolic pressure and a reduction of the diastolic pressure to 100 or below, 8 were receiving 1.0 to 1.25 gm. of sodium daily. None received less than 1 gm. of sodium daily. Allen,[12] Corcoran,[11] Grollman[13] and others have shown that when dietary measures alone are employed, the diet must contain 0.5 gm. of sodium or less to achieve twenty-four-hour urinary sodium levels of less than 0.5 gm. and to be generally effective in lowering the blood pressure.

The present study indicates that with the use of cation-exchange resins, sodium excretion of less than 0.5 gm. in twenty-four hours and a lowering of the blood pressure can be obtained with somewhat less rigid restrictions in the intake of sodium than are needed with dietary restrictions alone. But, if these results are to be obtained, sodium restriction cannot be completely abolished.

Additions of salt to the diet or substitutions for the resin of a placebo lead to increases in the blood pressure. The increases in blood pressure following the substitution of a placebo for the resin or the additions to the intake of salt were most marked in the cases in which the lowest urinary sodium excretions had been obtained by means of resin therapy. In addition, increase in body weight and the return or increase of symptoms, notably headache and nervousness, were most pronounced in the cases in which the placebo or extra salt was given. These changes were accompanied by an increased sodium excretion in the urine — usually to more than 0.8 gm. per twenty-four hours. The course of 1 patient whose blood pressure is especially sensitive to the restriction of sodium is shown in Figure 1. She had a Grade II hypertension and now maintains a normal blood pressure while receiving a diet containing 1 gm. of sodium with resin therapy — 45 gm. daily, while excreting a urinary

TABLE 3. *Correlation of Changes in Blood Pressure and Urinary Sodium in Patients Receiving Diets Restricted in Sodium and with Resin.**

24-Hr. Urine Sodium	Mean Drop in Diastolic Blood Pressure					
	20 or more	10–19	0–9	None (increase)	To 100 or less	Both 20 or more and to 100 or less
gm.						
0.5	10	3	1	1	7	6
0.5 to 0.9	3	4	2	0	7	3
1 or more	2	4	5	3	3	0
Total (38 cases)	15 (39%)	11 (30%)	8 (21%)	4 (10%)	17 (45%)	9 (24%)

*The smaller the amount of sodium in the urine, the greater the lowering effect on the blood pressure, and vice versa.

TABLE 4. *Effect of Low Sodium Intake Combined with Resin Therapy.**

Prescribed Dietary Sodium	Reduction of Diastolic Pressure		
	20 or more	To 100 or less	Both 20 or more and to 100 or less
gm.			
1–1.25	14	12	8
1.5	1	3	1
2		2	
Totals	15	17	9

*The smaller the intake of sodium, the greater the reduction in diastolic blood pressure.

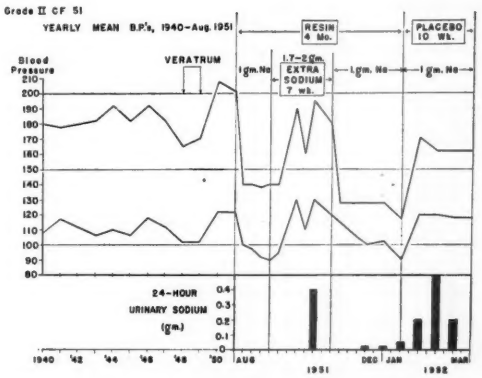

FIGURE 1. *Course in a Fifty-One-Year-Old Woman Whose Blood Pressure Was Especially Sensitive to Restriction of Sodium.*

sodium of 0.1 gm. per twenty-four hours. An increase in the intake of sodium to 1.7 gm. daily (unknown to the patient) increased the urinary sodium to 0.38 gm. per twenty-four hours, and was followed by a rapid return of the blood pressure to the hypertensive levels maintained for the previous fourteen years and by a return of headache. When the sodium intake was reduced to 1 gm., a decrease in blood pressure and an alleviation of headaches ensued. After a suitable period, a placebo — indistinguishable to the patient from the resin — was substituted for the resin. The blood pressure promptly increased to 170 systolic, 120 diastolic.

The courses in 2 Negresses, aged forty-one and forty-nine years, each with Grade III hypertension,

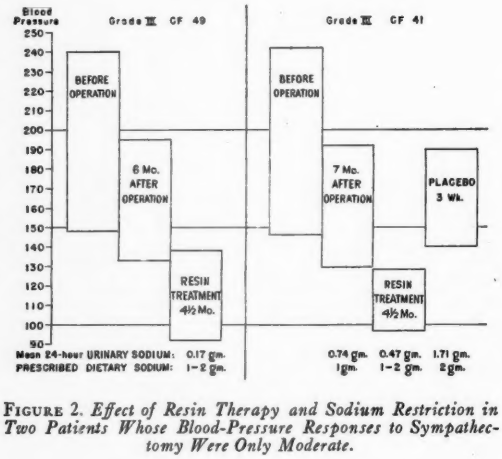

FIGURE 2. *Effect of Resin Therapy and Sodium Restriction in Two Patients Whose Blood-Pressure Responses to Sympathectomy Were Only Moderate.*

who had only modest blood-pressure responses to thoracolumbar sympathectomy are presented in Figure 2. Both had rapid, dramatic and sustained lowering of the blood pressures while receiving cation-exchange resins and low-sodium diets. They required less sodium restriction than the other patients in this series and are now being carried on a 2-gm. intake of dietary sodium (see Table 1) and 45 gm. of resin daily and still have a urinary sodium of less than 0.5 gm. per twenty-four hours. Both had marked improvement in the ballistocardiographic patterns within a month of the start of resin therapy.

Most of the patients whose urinary sodium was constantly, or even intermittently, below 0.5 gm. per twenty-four hours experienced relief from headache, dizziness and palpitations whether or not the blood pressure was significantly lowered. Also, a loss of 3 to 5 pounds in body weight occurring in the first few weeks of resin therapy was a characteristic of this group.

Although complete follow-up studies of eye grounds, electrocardiograms and heart sizes are not yet available, after four to ten months of therapy, 10 of 26 patients demonstrated regression of eyeground changes as classified by Keith, Wagener and Barker[9]; there was less arterial spasticity with disappearance of hemorrhages and exudates; 6 of 27 patients showed slight changes in the electrocardiographic pattern characterized by a more normal appearance of ST segments and T waves; and 10 of 26 patients had slight decreases in transverse cardiac diameters. In 7 of 10 patients the ballistocardiographic patterns have improved, and 5 of 7 have demonstrated improved phenolsulfonphthalein excretion. At present no correlations of blood pressure, funduscopic, electrocardiographic or cardiac changes are practicable.

Complications of Resin Therapy

Constipation, anorexia and a sensation of abdominal fullness were common complaints early in the course of treatment, but these symptoms gradually subsided. Many patients reported that their stools were hard, dry and gritty. Many complained of the unpalatability of the resin, but none who had previously received rice or other diets low in sodium content or veratrum viride therapy chose to return to those regimens. They were willing to accept the resin, the palatability of which has recently been improved, to have a more practicable diet.

Hyperchloremia, elevations of the blood urea nitrogen, acidosis and hypopotassemia, all of mild degree and occasionally accompanied by weakness and malaise, have been encountered. No case of frank uremia nor of hyperpotassemia has occurred, but hyponatremia, hypocalcemia and severe hypopotassemia, with marked asthenia, each occurred once before we had adopted the routine of prescribing potassium citrate and calcium lactate. In each case, the patient had stopped eating because of asthenia and anorexia, but had continued to take resin. These disturbances cleared up promptly with the resumption of full diets and extra rations of the electrolytes involved. In only 4 cases — and this was in the early phases of the study — was it necessary to discontinue the resin temporarily because of these electrolyte difficulties, and no patient had to be removed permanently from the study for these reasons.

The occurrence of hypopotassemia is probably due to three factors: excretion of potassium in the urine with the excess chloride ions; the tendency of low-sodium diets to be low in potassium; and potassium absorption by the resin despite its potassium content.

It should be noted that asthenia and malaise and nausea do not necessarily indicate sodium depletion, but may indicate potassium depletion, especially if the blood pressure is elevated during the occurrence

of these symptoms. We believe that the limited selection of patients with no great loss of renal function accounts in large part for the few cases of severe electrolyte disturbances and their concomitant signs and symptoms.

The imbalance of electrolytes is corrected or prevented by the administration of calcium lactate, 2 gm., and potassium citrate, 2 or 3 gm., daily. These measures also minimize the tendency to hyperchloremic acidosis by providing basic ions to be excreted with the excess chloride. Electrolyte disturbances tend to be more severe, and development of weakness and malaise is more likely, if there is a rapid lowering of the blood pressure (within a week) than if the response occurs over a longer period.

Discussion

Corcoran, Taylor and Page[11] have shown that diets low in sodium were accompanied by significant lowering of the blood pressure in about 25 per cent of hospitalized patients and in a much lower percentage of ambulatory hypertensive patients. They believe that low-sodium-diet therapy is not very practical for outpatients. Our study to date indicates that cation-exchange resins, when used in conjunction with diets containing 1 to 1.5 gm. of sodium daily (Table 1), are of pronounced value in obtaining the sodium restriction required to lower the blood pressure in nonhospitalized hypertensive patients whose blood pressures are sensitive to a restricted intake of sodium.

The use of cation-exchange resins to divert sodium from the body and to lower the blood pressure in the so-called "salt-sensitive" hypertensive patient adds to the current concept that the sodium rather than the chloride ion is important in regulating the blood pressure in this group of patients.

Once the blood pressure has been lowered by appropriate restrictions in the sodium intake, it frequently rises only slowly over a period of days or weeks after the discontinuance of this restriction. It may be practicable, therefore, to use resins intermittently with rest periods of several days between courses of resin ingestion in some patients. This will need to be a highly individualized procedure with the physician becoming intimately acquainted with the response pattern of each patient, and interrupted therapy will not be possible in all cases. Since the absorptive capacity of the resins decreases after several days of use, a rest period might serve to allow the resins to act with their maximal in vivo capacity again upon resumption of their use.

If a patient with essential hypertension has a normal urinalysis, a normal concentrating power or phenolsulphonphthalein excretion test or, failing these, a normal blood urea nitrogen, he may safely be given a trial of cation-exchange resin and restricted dietary sodium therapy. During the course of this therapy, interval determinations of blood urea nitrogen and carbon dioxide combining power should suffice for practical purposes to follow the course of blood chemical changes, as long as supplementary calcium and potassium ions are given. If the blood pressure does not decrease during the course of therapy, the twenty-four-hour output of urinary sodium will be needed to determine whether or not the sodium is being sufficiently restricted for a blood-pressure drop to occur.

Summary and Conclusions

Cation-exchange resins are effective adjuncts to diets low in sodium content but are not substitutes for them in the management of properly selected patients suffering from essential hypertension. With the resins, diets containing 1.0 to 1.25 gm. sodium can be utilized instead of the levels of 0.2 to 0.5 gm. needed with dietotherapy alone. Thus, dietary palatability and patient co-operation are increased.

Deficiencies in serum calcium and potassium, which sometimes occur as the result of this therapy, may be prevented by the administration of supplements of calcium lactate and potassium citrate. This measure also serves to minimize the tendency to hyperchloremic acidosis.

These studies strengthen the claims of those who believe that the reduction of sodium has an important place in the treatment of essential hypertension. The easier and more intense sodium restriction attained by the sodium-removing properties of the cation-exchange resins increases greatly the number of nonhospitalized patients with hypertension who may be benefited.

The dramatic benefit from cation-exchange-resin therapy in patients whose hypertension had not responded adequately to a sympathectomy is recorded. It is suggested that the addition of such therapy to the restriction of sodium may salvage a considerable percentage of these patients with intractable hypertension.

A trial of cation-exchange resin and restricted dietary sodium therapy may safely be given to a patient with essential hypertension if he has at least moderately good renal function as indicated by the urinalysis, the phenolsulfonphthalein excretion test or urine concentration test, and the blood urea nitrogen determination.

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BULBAR POLIOMYELITIS

MAX J. FOX, M.D.,* J. F. KUZMA, M.D.,† AND C. L. JUNKERMAN, M.D.‡

MILWAUKEE, WISCONSIN

THIS report is an analysis primarily of the incidence and prognosis of the various syndromes usually grouped together under the general term "bulbar poliomyelitis." The bulbar forms of acute poliomyelitis account for most of the deaths in the disease; therefore, an important approach to the reduction of the mortality rate is through better understanding of these forms. For this reason, reports[1-3] on the Minnesota epidemic of 1946 divided the bulbar forms into various subdivisions and suggested that they consisted of not one but several distinct clinical and pathological entities. Since rational therapy must depend on the type of bulbar involvement present in the individual patient, this toxonomic subdivision is justified.

Two factors tend to decrease the statistical significance of a single epidemic of poliomyelitis in a particular community. One of these is the variation in the pattern of epidemics from year to year, and the other is the difficulty in accumulating a numerically significant group of cases in any single local epidemic. To minimize these factors, an analysis of 1863 cases, occurring over a twelve-year period, is presented. These figures represent the total number of cases of poliomyelitis admitted to South View (Isolation) Hospital in Milwaukee, Wisconsin, during the years 1940 through 1951.

TYPES

By a modification of Baker's[3] classification of bulbar poliomyelitis the heterogeneous term "bulbar" is qualified by subdivision into clinically distinct entities. The value of such a classification is immediately apparent since the mortality rates in the subgroups vary widely and, as pointed out by others,[3] the treatment differs, depending on which manifestation of bulbar involvement is dominant. The overlap of subgroups is at times considerable, making strict definition difficult in some cases. Thus, a patient with evidence of marked respiratory-center damage and some signs of involvement of the nucleus of the tenth cranial nerve would be placed in the respiratory type of the bulbar-central autonomic group. The subgroup classification of bulbar poliomyelitis based on the predominant manifestation is as follows:

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†Assistant professor of pathology, Marquette University School of Medicine; director of laboratories, Milwaukee County Institutions.
‡Resident in internal medicine, Columbia Hospital.

Bulbar-Encephalitic

The *diffuse* form of encephalitis characterized by great apprehension, rapidity of ideas, hyperactivity, confusion, irrationality and coma was the predominant clinical picture in 33 (8 per cent) of 415 patients, 7, or 21 per cent, of whom died. Because cerebral hypoxia is almost indistinguishable from the virus involvement of the cortex, selection of cases for this category was difficult. Many of these patients, however, continued to show signs of diffuse encephalitis when the airway was clear and supplemental oxygen was given. The *focal* encephalitic group is identified by evidence of focal cerebral involvement such as aphasia, spastic hemiparesis, myoclonic jerking or convulsions, or all four, and was observed in only 4 cases (1 per cent), of which 1 was fatal — a mortality of 25 per cent.

Bulbar-Central Autonomic

The bulbar-*respiratory* center group shows predominance of signs of respiratory center failure. The respirations are usually shallow and irregular. Terminally, there is increasing cyanosis, tachypnea and evidence of hypoxia, even when the patient has an adequate airway, as well as pneumotoxic, apneumatic and gasping depot disturbances. Failure of the respiratory center was the predominant feature in 39 cases (9 per cent). Of these, 38, or 98 per cent, proved fatal. In most of these patients the diaphragm and intercostal muscles were functioning, and death resulted from central failure; however, in some cases the action of the diaphragm and intercostal muscles was impaired but it was believed that the predominant factor was central failure of respiration. The bulbar-*circulatory* center group consists of patients in whom signs of circulatory center failure are the most prominent feature. The usual findings are rapid, weak and irregular pulse and marked hypotension. We have also noted that a fair percentage of these patients have an essential hypertension, especially hypertensive diastolic readings. Terminally, there is complete circulatory

failure. Often the heart tones become inaudible before respiration ceases. Twenty-three patients (6 per cent) were classified in this group, with 21 deaths — a mortality of 92 per cent.

Bulbar-Cranial

Involvement of the *upper cranial nerves* occurred in 30 cases (7 per cent). It is not surprising that there were no deaths because these nerves are not essential to life. The nucleus of the seventh cranial nerve was most commonly affected, as evidenced by facial-nerve paralysis of varying degree and extent. Ocular palsies, nystagmus and vertigo were rarely observed in this series. Damage to the nuclei of the *lower cranial nerves*, particularly the tenth, constituted a definite threat to life. Of 123 patients (30 per cent) whose predominant signs placed them in this group, 25, or 20 per cent, died. The problem in these cases is the maintenance of an adequate airway, which is threatened by the accumulation of secretions that the patient is unable to swallow and, in some cases, by reflex spasm of the glottis or abductor paralysis of the vocal cords. It is probable that careful observation of the patient, anticipation of the complications and early tracheotomy in selected cases will reduce the mortality rate in this group.

Bulbar-Spinal

The clinical picture of both bulbar and spinal-cord involvement was observed in 163 patients (39 per cent). Of these, 41, or 25 per cent, died. Death occurred in the cases in which impairment of the intercostal muscles and diaphragm was present. In this group the problems of respiratory embarrassment or central damage were further complicated by the inability of the patient to use his accessory muscles, thereby necessitating the use of a respirator. The prognosis was much better in the cases in which there was impairment of action only of muscles other than those of respiration.

Incidence

The material for this study consisted of 1863 cases of poliomyelitis. Any case with bulbar signs was placed in the bulbar group for further review regardless of the presence or absence of co-existing spinal-cord involvement (Table 1). There were 415 cases of the bulbar form of poliomyelitis, an incidence of 22.2 per cent. This figure represents the incidence over a twelve-year period, and is considerably higher than that found in previous reports, with the exception of that of Grulee and Panos,[4] in which the incidence was 23 per cent in 464 cases, and that of Piszczek,[5] in which the incidence was 20.8 per cent in 1300 cases.

There were 134 deaths, a mortality of 7.2 per cent for the entire series. All but 1 of these deaths occurred in patients with bulbar involvement. The cause of the remaining death, occurring in the spinal-paralytic group, was not determined by autopsy but was probably not related to poliomyelitis. It is quite apparent that any decrease in the mortality of poliomyelitis must stem from further investigation of the bulbar forms.

When the 415 cases classified in Table 1 as bulbar cases were considered in relation to the presence or absence of *concomitant spinal-cord involvement*, 218, or 52.5 per cent, were found to be strictly bulbar and showed no spinal-cord involvement (Table 2). The remaining 197 patients had coexistent bulbar signs and clinical indications of spinal-cord disease.

Table 1. *Incidence and Mortality, by Years, in 1863 Cases of Poliomyelitis.*

Year	Nonparalytic Cases	Spinal-Paralytic Cases	Bulbar Cases	Total Cases	Total Deaths	Mortality	Mortality in Bulbar Cases
						%	%
1940	5	25	12	42	5	12	29.0
1941	2	0	0	2	0	0	0
1942	1	8	0	9	0	0	0
1943	4	19	12	45	3	7	27.0
1944	24	46	21	91	9	10	23.0
1945	78	102	41	221	16	7	19.0
1946	80	70	58	208	7	3	28.0
1947	87	0	0	87	0	0	0
1948	122	59	93	274	41	15	34.0
1949	67	66	49	182	12	7	27.0
1950	69	109	54	232	10	4	23.2
1951	204	191	75	470	31	7	15.9
Totals	753	695	415	1863	134		
Averages						7.2	22.2

Table 2. *Incidence of Spinal-Cord Involvement.*

Type of Poliomyelitis	No. of Cases	Percentage	No. of Deaths	Mortality
				%
Strictly bulbar	218	52.5	68	31
Bulbar and spinal cord	197	47.5	65	33
Totals	415		133	
Averages		100.0		32

The mortality in this group of cases with bulbar and spinal-cord involvement was 33 per cent, not significantly greater than the 31 per cent mortality in the strictly bulbar cases and not as great as the difference reported by Piszczek,[5] in whose series the mortality rate for patients with bulbar and spinal-cord involvement (46 per cent of 63 cases) was almost twice that for strictly bulbar cases (23.2 per cent of 207 cases).

Table 1 illustrates the variability of the disease. In three of the years there were no bulbar cases. In 1941 and 1942, this was probably because of the low total case incidence, but in 1947 there were 87 cases, all of which were nonparalytic. Although the bulbar cases accounted for almost the entire mortality rate, the mortality per given epidemic was not proportional to the incidence of the bulbar disease. For example, in 1946 there was a higher than average incidence of bulbar cases and a lower than average mortality. The total number of cases in any one year, the severity of the individual cases and the incidence of the bulbar form are apparently unrelated.

Table 3. *Incidence of Various Manifestations.*

Manifestation	No. of Cases	Percentage
Encephalitis	77	18.5
Involvement of 7th cranial nerve	116	28.0
Involvement of 10th cranial nerve	328	79.0
Circulatory failure	33	8.0
Respiratory failure	66	15.9

Manifestations

Table 3 records the most common manifestations of the bulbar types as seen in this series. The number of cases and the percentages in which these findings occurred are presented regardless of whether they formed a dominant or subordinate feature of the illness. In that respect the manifestations differ from the subgroup classifications presented above, which referred to the outstanding features of the illnesses.

Signs of encephalitis were present in 77, or 18.5 per cent, of the 415 bulbar cases. The most frequently involved cranial-nerve nucleus in the entire bulbar group was that of the tenth nerve — 328, or 79 per cent, of the patients showed this defect. Facial-nerve weakness or paralysis was second in frequency, being noted in 116 patients, or 28 per cent. Signs of autonomic-center failure were found in 62 (15 per cent).

Incidence According to Age

Of the patients in the 415 bulbar cases 82 per cent were under twenty-one years of age, and of those in the 1448 nonbulbar cases, 87 per cent. However, only 49 per cent of the bulbar cases were in patients under eleven years of age, in contrast to 65 per cent of nonbulbar cases in patients in the same age range, indicating that a greater proportion of the bulbar than other forms occurred in patients ten to twenty years of age. The age range in the bulbar cases was eleven months to fifty-three years, and that in the nonbulbar cases from six weeks to sixty-four years (Table 4).

Incidence According to Sex

In this series there was no appreciable difference in the sex incidence between bulbar and nonbulbar groups. This is at variance with the report of Grulee and Panos,[4] in which the incidence of the bulbar form in males was significantly higher than that in females. In both groups slightly over half the cases were found in males. (Table 4).

Table 4. *Incidence according to Age and Sex.*

Type of Poliomyelitis	Total Cases	Patients under 11 Yr. of Age	Patients under 21 Yr. of Age	Female Patients	Male Patients	Deaths among Female Patients	Deaths among Male Patients
Bulbar	415	203 (49%)	341 (82%)	175 (42%)	240 (58%)	58 (43.5%)	75 (56.5%)
Nonbulbar	1448	945 (65%)	945 (65%)	630 (43%)	818 (56%)	1 (0.07%)	0

Cerebrospinal-Fluid Cell Counts

Table 5 shows the range of cerebrospinal-fluid cell counts in 385 bulbar and 1396 nonbulbar cases.

Table 5. *Cerebrospinal-Fluid Cell Counts.*

Cell Count	Bulbar Cases		Nonbulbar Cases	
	No. of cases	Percentage	No. of cases	Percentage
per cu. mm.				
0-9	11	3	64	5
10-20	31	8	152	11
21-50	83	22	286	20
51-100	96	25	306	22
101-200	101	26	335	24
201-300	36	9	126	9
Over 300	27	7	127	9
Totals	385		1396	

There was no significant difference between the cell counts in the two groups. As in a previously reported series[4] most of the counts fell in the range of 20 to 200 cells per cubic millimeter. The highest count in the bulbar group was 1092 cells and the highest in the nonbulbar (nonparalytic and spinal-paralytic) cases was 3000 cells per cubic millimeter. Only 5 patients in the entire series had counts of

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more than 1000 cells. There was no correlation between the severity or type of disease and the total or differential cerebrospinal-fluid cell count.

Pathological Findings

In recent times an attempt has been made to correlate the clinical and pathological features of bulbar poliomyelitis.[3, 6-8] Particularly significant contributions in this respect are the reports of the Minneapolis investigators and their emphasis on the nature of the cell population in the anatomic sites involved in bulbar poliomyelitis.[1, 2, 3, 8] They have been able to judge the function of certain cells of the medulla according to the clinical findings when such cells are affected by the disease.

During the period covered by this report we have studied the central nervous system in 66 autopsied cases. Distribution of lesions is principally in the medulla, midbrain, spinal cord, cerebellum and motor cortex. This is especially characterized by interstitial inflammation of lymphocytes and polymorphonuclear cells coupled with frequent petechial hemorrhages. In 6 cases there was additional focal necrosis of the brain substance, which in 2 cases was accompanied by phagocytic macrophage cellular reaction. The interstitial inflammation and its site do not correlate very closely with the clinical findings. Neuronal changes, although without constant correlation, give the best clinicopathological appreciation. The best correlation is seen in the bulbar lower cranial group of patients with the involvement of nucleus ambiguus and nuclei of the eleventh and twelfth cranial nerves. This correlation is present in more than 50 per cent of the cases. Bulbar-spinal clinicopathological correlation according to cervical, thoracic and lumbar areas is excellent when one is interpreting the clinical manifestations according to pathologic change of the motor neurons of various spinal-cord segments. The bulbar-encephalitic group has meager correlation. The cortical changes were seen only in a few cases in contrast to the findings reported by Luhan[6]; however, nonspecific changes of hyperemia and edema were frequent. The bulbar-autonomic group is the most interesting one. Involvement in such cases is predominantly in the reticular area of the medulla. The ventral medial portion of the reticular area when chiefly involved is clinically manifested by circulatory disturbances, whereas involvement of the ventral lateral portion has chief effect upon respiration. Correlation in this group was about 30 per cent, but admittedly the reaction in this part of the medulla is frequently so severe as to make it difficult to separate medial and lateral changes.

Discussion

The clinical manifestations of bulbar poliomyelitis are associated with corresponding central-nervous-system changes that make an accurate clinicopathological correlation possible in a high percentage of cases. However, the correlation is frequently made difficult by poor neurologic examination of critically ill patients and inability to assess carefully the function of one part of the central nervous system in the face of such widespread damage. From a morphologic standpoint interstitial inflammation, although most severe, does not correlate as well as the neuron changes do, but even here morphologic change cannot always be directly translated into terms of functional ability. Clinicopathological correlation is at times difficult but nevertheless should be attempted since effective therapy in the clinical case depends upon it. The use of the respirator, tracheotomy, bronchoscopy, oxygen under pressure, antibiotics, sedation and so forth can be more effectively carried out if the patient is carefully evaluated and classified according to one of the subgroups of bulbar poliomyelitis.

Summary and Conclusions

Review of 1863 cases of poliomyelitis observed from 1940 through 1951 revealed that 415 (22.2 per cent) were of the bulbar type. All the deaths, except 1, occurred in the bulbar cases.

The division of bulbar cases into the following subgroups is of clinical value in determining prognosis and appropriate therapy: bulbar-encephalitic, diffuse and focal; bulbar-central autonomic, respiratory and circulatory; bulbar-cranial-nerve nuclei, upper and lower; and bulbar-spinal.

The largest single bulbar subdivision was the bulbar-spinal group, containing 163 patients.

The highest mortality occurred in the bulbar-autonomic-center group. Although only 15 per cent of the bulbar cases were in this category, they accounted for 44.3 per cent of the deaths in the entire series.

The lower-cranial-nerve-nuclei group was second in mortality incidence. It represented 30 per cent of the bulbar cases, with a mortality of 20 per cent.

Diffuse bulbar encephalitis was present in 33 patients, 21 per cent of whom died.

A correlation of the findings of 66 post-mortem examinations made during the course of this study is presented.

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PROGNOSTIC SIGNIFICANCE OF THE EPINEPHRINE TEST IN PREOPERATIVE PATIENTS*

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THIS paper presents an evaluation of the epinephrine test from the standpoint of its prognostic significance in patients being prepared for surgery, as well as a brief review of its use in the diagnosis of diseases of the pituitary-adrenal axis.

In 1908 Babes and Jonescu[1] observed that stress in man caused a decrease in suprarenal lipid and that multiple intravenous injections of epinephrine produced the same depletion. After Vogt's[2] demonstration in 1944 that epinephrine increased the content of the cortical hormones in the plasma of the renal vein of dogs and her subsequent observations[3] and those of Long and Fry[4] in 1945 that this action was abolished by hypophysectomy, numerous studies were initiated to determine possible clinical application of these phenomena.

Long and his associates,[5] in 1947, demonstrated that epinephrine, as well as certain stressful and traumatic conditions, produced a fall in adrenocortical ascorbic acid and cholesterol content. Further, they showed that this response was abolished in hypophysectomized animals, even though the adrenal cortex was maintained by ACTH injection subsequent to hypophysectomy. They reasoned, therefore, that the absence of the response following hypophysectomy was not due to secondary atrophy of the adrenal cortex, as suggested by Vogt,[2, 3] but to the loss of the hypophysis itself.

In an effort to establish the method by which epinephrine effects the release of ACTH from the anterior pituitary body numerous studies were carried out, resulting in a multitude of theoretical possibilities. Soskin[6] and Chi-Ping Cheng[7] believe that epinephrine stimulates the release of ACTH by increasing the peripheral utilization of cortical hormones. Hume[8] and Hume and Wittenstein[9] support the theory that ACTH release is initiated by a hormonal mechanism in the anterior hypothalamus, which, when activated by stress, will release a substance capable of causing an increased secretion of ACTH by the anterior pituitary body. Ingenious experiments were devised to support their contentions. Gershberg et al.[10] present evidence to support the theory that two mechanisms are responsible for cortical stimulation: an immediate response requiring epinephrine and a delayed component not requiring epinephrine. Both these effects were believed to be mediated via the anterior pituitary body. McDermott, Fry, Brobeck and Long[11] believed that ACTH release was produced by an autonomic mechanism mediated via the nervous system and a metabolic mechanism mediated by the rate of utilization of cortical hormones by the peripheral tissue. McDermott and his associates[12] showed that ACTH release was initiated by direct application of epinephrine to anterior pituitary tissue. Other theories have been offered with considerable experimental evidence in their support.[13-19] Conclusive evidence is not yet available to demonstrate the exact mechanism responsible for the release of ACTH from the anterior pituitary body, though it appears that numerous factors may be responsible.

Selye[20] and Selye and Dalton[21] demonstrated that eosinopenia constituted a characteristic part of the alarm reaction, and subsequent observations indicated that it was probably the most sensitive indicator of adrenocortical activity.[22]

With the increasing awareness of the part played by epinephrine in stimulating the anterior pituitary body, Recant, Forsham and Thorn[23] and Laragh and Almy,[24] working independently in 1948, showed that epinephrine failed to produce significant eosinopenia in patients with hypopituitarism and Addison's disease. Both groups proposed that the response to epinephrine might be used as a diagnostic aid in these conditions.

Continuation of this work by Recant et al.[17] enlarged on their experience and added support to their original observations. It was further demonstrated that certain anterior-hypothalamic lesions abolished the adrenocortical response to epinephrine. In combination with the ACTH test for adrenocortical insufficiency, as devised by Thorn and his co-workers,[25] epinephrine as an activator of the anterior pituitary body could be used to differentiate hypopituitarism and Addison's disease, as proposed by Recant, Forsham and Thorn[23] in 1948. Roche, Thorn and Hills,[26] in 1950, utilized the blood eosinophil response to ACTH and epinephrine in the determination of the fitness of 2 patients with Cushing's disease for surgery. Results were so encouraging that they later recommended this test in the selection and preparation of all patients for major operations.[27, 28] At about the same time, Recant et al.[17] demonstrated that in a hypophysectomized dog, whose adrenal cortex was maintained by ACTH, a stressful situation (nephrectomy) failed to produce a decrease in circulating eosinophils. ACTH, however, caused an eosinopenia. Roche and his associates[26] stated that the integrity of the adrenal cortex was essential for survival during major surgical operations. It has been shown that the stress of surgery may fail to initiate the mechanisms responsible for the stimulation of the adrenal cortex,

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because of failure at the hypothalamic, pituitary or adrenocortical level.[29]

The role of the hypothalamic-pituitary-adrenocortical axis in determining the patient's reaction during and his subsequent course after operation has not been determined. Selye et al.,[30] working with rats, concluded that increased cortin production plays an important role in shock resistance and that the symptoms and signs of shock are at least in part due to a relative adrenal insufficiency.

With these observations in mind we carried out a study in an attempt to determine if there was any correlation between the response of a patient's circulating eosinophils after the epinephrine test and his reaction to operation.

Method

Patients were selected from those being prepared for elective operations at the Charity Hospital of New Orleans. Patients who were to have only minor surgical procedures were eliminated from the study, because of the possibility that such procedures would not be sufficiently traumatic to initiate the "alarm reaction." A detailed history was taken from each patient in an attempt to eliminate from the study those with severe hypertension, cardiac disease and hyperthyroidism, which have been listed as contraindications by other authors.[31-33] No patients with a history compatible with adrenal insufficiency, hypopituitarism, hypothalamic disease, tuberculosis, allergic disorders, parasitic infestations, severe liver disease, ulcerative colitis, rheumatic fever, rheumatoid arthritis or severe emotional disturbances were included in this study, since various authors have reported an increased number of abnormal responses in these conditions.[34-37] No attempt was made to select patients according to age, sex, race or duration of illness. Four-hour epinephrine tests, using 0.3 cc. of 1:1000 epinephrine,* were carried out on 63 patients, according to the method described by Thorn,[32] with a modification of the Randolph stain[38] for enumerating eosinophils. Suggestions of Best and Samter[39] were followed to minimize technical errors.

Results

The fasting eosinophil levels determined on 63 patients in this series ranged from 47 to 1077 per cubic millimeter, with a mean of 224. This compares favorably with levels reported by other authors.[40-42]

After the administration of epinephrine, 20 of the 63 patients (32 per cent) showed a decrease of less than 50 per cent in circulating eosinophils, and 43 of the 63 (68 per cent) showed a decrease of 50 per cent or more. The mean decrease was 53 per cent.

Of the 20 patients showing less than 50 per cent decrease in circulating eosinophils, 7 remained in the hospital sufficiently long before operation for a second test. In 4 of these 7 no decrease of 50 per cent or more was obtained on the second test, whereas 3 revealed a decrease of greater than 50 per cent on retesting.

Of the 63 patients tested preoperatively, 45 were available for eosinophil counts on the first postoperative day. Only 3 of these showed a decrease in eosinophils less than 50 per cent of the preoperative control levels. In 1 of the 3 the preoperative response had been less than 50 per cent.

Of the 45 patients, there were 12 in whom a 50 per cent decrease in eosinophils was not obtained before operation. Three of these had demonstrated an abnormal response on two occasions. In this group of 12 patients with a subnormal preoperative response to epinephrine, 5 (42 per cent) showed a fall in blood pressure to shock levels during operation. For the purpose of this paper shock is defined as a lowering of the blood pressure of sufficient magnitude to require that remedial measures be instituted. In all cases this level was below 90 systolic. It is understood that this degree of hypotension does not represent the full-blown picture of shock and that, unattended, these patients might not have developed clinical shock. However, these criteria appeared most satisfactory for the purposes of the experiment. Of the 3 patients who had two subnormal responses preoperatively, 1 went into shock, 1 had an uncomplicated operative course, and 1 showed a considerable decrease in blood pressure, though not to shock levels.

Of the 33 patients with normal preoperative responses to epinephrine, 11 (33 per cent) had a decrease in blood pressure to shock levels. No complications other than shock were encountered in any patients during operation.

Of the patients with a subnormal preoperative response, only 1 had a postoperative complication (abscess and fever). In the group showing normal preoperative responses, 1 patient died in congestive heart failure on the second postoperative day (autopsy revealed old, undiagnosed rheumatic heart disease), and 1 died on the fifth postoperative day of an episode believed to be due to a pulmonary embolism (no post-mortem examination was performed).

Discussion

The number of abnormal responses to the epinephrine test in this series was surprisingly high (30 per cent); however a review of the individual responses in Ferguson's[43] series of controls revealed a similar high number of abnormal responses (30 per cent). Laragh,[24] working with normal subjects, reported an average decrease of 56 per cent after the epinephrine test, which very nearly approximated that of 53 per cent found in our series. Because of the frequency of apparently abnormal responses in normal persons, Best and his associates[44, 45] have reiterated the warning, "repeated failure to respond

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to epinephrine or ephedrine cannot be construed as indicating adrenal, pituitary or hypothalamic disease." Observations made in this study lend support to this statement, indicating that little, if any, significance should be attributed to abnormal responses to the four-hour epinephrine test. In the light of these findings and those of Thorn and his associates,[46] in which normal responses were obtained in 4 of 34 patients with Addison's disease, it seems wise to interpret any four-hour epinephrine test, whether normal or abnormal, with extreme caution.

Complications of surgery, though present in 4 per cent of the patients who showed an abnormal response to the epinephrine test in this series, do not seem to occur significantly more frequently in those with an abnormal response than in those showing a normal response to the epinephrine test prior to operation.

Of the circulating eosinophil levels determined on the first postoperative day, only 3 patients of 45 showed a decrease of less than 50 per cent, as compared to their preoperative fasting levels. All 3 made uneventful recoveries. This does not seem to support the contention of Roche et al.[27, 47] that a high postoperative eosinophil level suggests adrenocortical insufficiency. One should consider, however, that in these 3 patients the trauma may not have been of sufficient severity to call forth a maximum adrenocortical response. In view of the fact that 1 of these patients had a vaginal hysterectomy with anterior and posterior repair of two hours' duration, another had a laparotomy with freeing of adhesions of an unknown duration, and a third had an abdominal hysterectomy with a bilateral salpingo-oöphorectomy lasting two hours and seven minutes, it is believed that such an argument is not valid. The operation on the first of the patients mentioned above was carried out under spinal anesthesia, the only case in this series in which spinal anesthesia was used. The high postoperative eosinophil level may well have been a result of the spinal anesthesia, for Hume and Wittenstein[9] have shown that spinal-cord lesions interfere with the organism's normal response to stress. Such an explanation does not seem to explain adequately the response obtained on the 2 remaining patients.

One patient in this series had a pituitary adenoma removed surgically, after a normal response to epinephrine. This observation lends support to the statement that significant eosinopenia was seen in patients with demonstrable lesions of the pituitary or hypothalamus.[44, 45] However, these authors do not describe the type or extent of the pituitary lesions with which they worked. In this regard, it seems noteworthy that we have found no reports of normal responses to the four-hour epinephrine test in patients known to have hypopituitarism.

Summary and Conclusions

In an attempt to evaluate the usefulness of the four-hour epinephrine test as a prognostic aid in preoperative patients, a series of epinephrine tests was run on patients being prepared for elective major operations. A short chronologic outline of the advancements in endocrinology that led to the development of the epinephrine test as an indicator of hypothalamic-pituitary-adrenocortical function is given. Results obtained in this study are discussed and evaluated in the light of data obtained by other authors.

Although it is realized that this series is small, the four-hour epinephrine test seems to be of no prognostic value in preoperative patients.

Eosinophil counts obtained on the first postoperative day do not seem to be of value in predicting the subsequent course of surgical patients.

Repeated failures to respond normally to the four-hour epinephrine test may occur in the presence of adequate adrenocortical reserve.

These data, in conjunction with information reported by other authors, indicate that the four-hour epinephrine test whether normal or abnormal must be interpreted with extreme caution, since normal responses have been obtained in patients known to have adrenocortical insufficiency and hypothalamic-pituitary lesions and patients known to have adequate adrenocortical reserve may show abnormal responses to the test.

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HYPERTROPHIC PULMONARY OSTEOARTHROPATHY SIMULATING RHEUMATOID ARTHRITIS*

Subsidence after Pneumonectomy for Carcinoma

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HYPERTROPHIC osteoarthropathy of severe degree is usually associated with cancer of the lung.[1-11] This association deserves emphasis, for the osteoarthropathy frequently antedates, occasionally by more than a year, the symptoms of the pulmonary lesion, which may be in its early stages.

In the case reported below, pulmonary osteoarthropathy was mistaken for rheumatoid arthritis. The inflammatory reaction about the bones and joints of the extremities was unusually marked. The unsuspected carcinoma of the lung was demonstrated by a chest film taken to investigate atelectasis after laparotomy for perforated duodenal ulcer. Serial x-ray study demonstrated the rapid progression of osteoarthropathy before pneumonectomy, and its disappearance within three months of operation. Two separate carcinomatous tumors were present in the lung.

CASE REPORT

R. I. (B.I.H. M19744), a 60-year-old man, was admitted to the hospital with the diagnosis of rheumatoid arthritis and internal derangement of the left knee. Four months prior to admission he sustained a fracture of the left patella, for which the left knee was immobilized for 2 months. After removal of the cast the knee remained painful and swollen. In the 2 months before admission, the right knee, both ankles and both wrists also became swollen and tender, and the patient noticed painless swelling of the fingertips. There were no pulmonary symptoms. Thirty-four years earlier he had been considered to have a peptic ulcer, but there had been no ulcer symptoms for 13 years before admission.

Physical examination disclosed a thin, sick man. There was swelling, tenderness, slight redness and increased warmth at both knees, ankles and wrists. The fingertips were distinctly clubbed and cyanotic. Examination was otherwise not

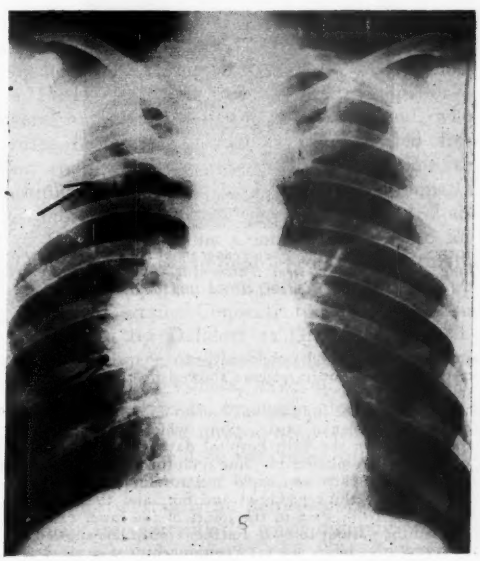

FIGURE 1. *Preoperative Roentgenogram of the Chest, Showing the Peripheral and Hilar Areas of Consolidation in the Right Lung.*

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remarkable. Examination of the blood showed a hemoglobin of 12 gm. per 100 cc., a red-cell sedimentation rate of 0.75 mm. per minute and a blood uric acid of 3.6 mg. per 100 cc.

The patient was given 1 gm. of aspirin and 1 gm. of sodium bicarbonate every 4 hours. On the 6th hospital day perforation of a duodenal ulcer occurred. The perforation was promptly closed. In the first 2 postoperative days the patient observed a marked amelioration of joint symptoms, which then recurred. A chest film, taken after operation because of left-lower-lobe atelectasis, also showed two areas of consolidation in the right lung — a peripheral round lesion in the upper lobe and a large irregular area of consolidation of the lung root. Subsequent chest films demonstrated clearing of the atelectasis but persistence of the masses in the right lung (Fig. 1). X-ray examination of the extremities revealed periosteal thickening and new-bone formation involving the metacarpals, the distal thirds of the radius, ulna, tibia and fibula bilaterally, and the shafts of both femurs (Fig. 2). The radiologist's diagnosis was hypertrophic pulmonary

FIGURE 2. *Preoperative Roentgenogram of the Left Forearm and Hand, Showing Periosteal Thickening and Calcification Involving the Radius, Ulna and Metacarpals.*

osteoarthropathy and pulmonary carcinoma. Bronchoscopy was negative. Sputum smears showed no tubercle bacilli or malignant cells.

Therapy for the lung lesions had to be deferred because of persistent duodenal obstruction, which required gastrojejunostomy on the 38th hospital day. Apart from a brief postoperative remission in joint symptoms the osteoarthropathy showed steady and rapid accentuation. The wrists and forearms were thickened, red and hot, and the fingers and wrists were stiff. Pain in the joints of the lower extremities confined the patient to bed. Further chest films showed rapid growth of the hilar mass. Pneumonectomy was therefore performed in spite of the patient's poor nutritional state.

At thoracotomy, a subpleural upper-lobe tumor and a separate hilar tumor were found as shown by the x-ray films. The hilar mass was largely intrapulmonary, however, so that vessels and bronchus could be divided well beyond the lesion. The pleura was free. Mediastinal lymph nodes showed no tumor. The pathologist reported a rounded, poorly circumscribed, well differentiated peripheral adenocarcinoma about 2.5 cm. in diameter, and a second carcinoma, firmer and better circumscribed but histologically undifferentiated, about 7 cm. in diameter, at the confluence of the lobes, compressing a major lobar artery.

The convalescence was uncomplicated. Regression of the osteoarthropathy was apparent during the 2d postoperative week. At discharge on the 16th postoperative day the redness and tenderness of the extremities had disappeared, and the patient was able to walk, free of pain except in the

FIGURE 3. *Roentgenogram of the Left Forearm and Hand Taken Three and One-Half Months After Pneumonectomy. No evidence of periostitis remains. A film taken six months later was identical.*

injured knee. Two months after discharge there was marked regression of periosteal calcification. A month later, clubbing was minimal, the fingertips were no longer cyanotic, and the x-ray appearance of the bones was normal (Fig. 3). Six months later he was in good health. The remaining lung, the bones and joints were normal, except for the left knee. The fingernails showed only slight convexity.

DISCUSSION

Awareness of the strong association of hypertrophic osteoarthropathy with malignant intrathoracic lesions will lead to the discovery of occasional cases of otherwise unrecognized pulmonary carcinoma in a resectable phase. Osteoarthropathy is commonly mistaken for arthritis, but this mistake will not be made if x-ray examination of the extremities is carried out.

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MEDICAL PROGRESS

THE IMPORTANCE OF COXSACKIE VIRUSES IN HUMAN DISEASE, PARTICULARLY HERPANGINA AND EPIDEMIC PLEURODYNIA (Concluded)*

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DISEASES PRODUCED BY COXSACKIE VIRUSES

Relation to Poliomyelitis and "Poliomyelitis-Like" Illnesses

Most important of the attributes of Coxsackie viruses is that of their relation to illness. Whether any or all of these viruses cause illness and, if so, what sort of illness are matters for careful consideration. It has already been pointed out that the viruses are found in many people in many parts of the world: their very ubiquity is therefore a factor of importance. Furthermore, their isolation from feces is a simple laboratory procedure; as a result, they have been widely, though usually sporadically, reported in persons suffering from a variety of clinical syndromes — including paralytic and nonparalytic poliomyelitis[1, 28, 29, 33, 34, 47, 50, 54, 56, 61-64, 73, 76, 77]; poliomyelitis-like syndromes[3, 29, 41, 67, 70]; "summer grippe"[49]; aseptic meningitis[28, 41]; "influenza-like illnesses"[73, 40]; fevers of unknown origin[3, 41, 55, 60]; syndromes with more or less protean symptoms[66, 71]; myalgia, epidemic pleurodynia or Bornholm disease[39, 43, 48, 54, 65, 68, 73, 78]; and herpangina.[23, 24] They have, however, also been isolated from persons not ill,[23, 24, 32] which immediately poses the question of the extent of inapparent infections and the possibility of confusing such an infection as the cause of the patient's signs and symptoms. Most studies have not been designed to answer this question, for testing has been restricted to a single category — that of the clinical picture being studied. Such investigations are therefore uncontrolled. Of some 50 papers dealing primarily with isolation of Coxsackie viruses or with their assumed relation to human disease, only 4 have utilized controls in the sense that adequate numbers of the healthy population, or even of persons with illnesses other than the one being studied, have also been examined in the same way in the same area or population group at the same time. The issue is further obscured by the tendency of many authors to report isolations of simply a "Coxsackie virus" as though it were a single entity; it is thus not apparent, when such an isolation is associated on inadequate evidence with a particular clinical picture, whether the strains of virus found are all alike, or whether they belong to Group A, Group B, to any one of the 15 known types within these groups or to several of these types. On the other hand, when viruses have been isolated and identified from what appears to be a single clinical syndrome, the multiplicity of types, and especially groups, is even more confusing — for example, Types 1, 2 and 4 of Group A, strains Connecticut 5, Ohio and Powers of Group B and ungrouped strain Matulaitis have all been reported from poliomyelitis, and Type 2, Group A, strains Connecticut 5, Demole, Kine (all classified by Dalldorf as Group B, Type 1), an untyped but probable Group A strain and ungrouped, untyped viruses, have all been found in cases considered to be epidemic pleurodynia. Although it cannot be unequivocally stated that all these viruses may not be associated, etiologically or in some other important way, with these diseases, there is most certainly no published valid evidence that they are, particularly when different workers have isolated such a variety of viruses from persons having the same clinical picture. The difficulty in assessing the etiologic significance of these viruses has been due chiefly to the lack of adequate controls. On the other hand, we believe that

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there is good evidence from controlled studies that multiple types *within a single group* (Group A) can and do cause a single clinically recognizable entity — namely, herpangina. There is evidence from other controlled studies — discussed below — that a Group B virus may indeed be responsible for epidemic pleurodynia.

Because the first isolations of Coxsackie viruses were made from patients with poliomyelitis,[1] and because of the physical and chemical similarities of these viruses to poliomyelitis, the latter disease has received the lion's share of attention. Many investigators have looked for Coxsackie viruses only during outbreaks of poliomyelitis; when, because of certain epidemiologic similarities to poliomyelitis viruses in seasonal occurrence, habitat and mode of spread, Coxsackie viruses were found, it was suggested that such viruses might cause diseases resembling poliomyelitis,[9, 28, 40, 41, 56, 63, 79] might influence the occurrence of paralysis in persons also harboring poliomyelitis virus,[34, 56, 80] or, somehow, in similar dual infections, might influence the occurrence or severity of an *epidemic* of poliomyelitis.[33] Most of these investigators have later qualified their initial impressions. However, when such implications have once appeared in print, they have been seized upon by numerous readers, have been repeated and extended in the introduction or discussion of almost every subsequent paper on Coxsackie viruses, and have thus given credence to hypotheses by sheer impact of reiteration.

Our extensive investigations of the occurrence of Coxsackie viruses, including approximately 400 isolations from more than 7000 specimens collected from 1949 through 1951, and including poliomyelitis, provide little basis for the hypothesis that any of the viruses encountered were producing illnesses likely to be confused with the clinical syndromes ascribed to infection with poliomyelitis virus. In none of the areas in which these studies were performed was there an excessive occurrence of poliomyelitis, and hence there was no great predilection on the part of physicians to consider mild febrile summer illnesses as poliomyelitis infections.

During these studies, our surveillance of the respective communities and hospital groups was such that we were able to examine the feces of a large proportion (and in some instances a majority) of poliomyelitis and poliomyelitis-like cases for Coxsackie viruses. Thus, in collaborative studies with the Children's Hospital Research Group during 1950 and 1951, 246 cases of poliomyelitis were studied for Coxsackie virus. In 1950, single stool specimens taken on admission to the hospital were obtained in 170 cases, none of which were positive for Coxsackie virus.[7, 23] In 1951,* 246 stools were obtained from 76 patients with poliomyelitis, including fecal specimens obtained on admission and usually at least two subsequent specimens. Coxsackie viruses were recovered from only 5 specimens obtained from 3 patients. It was most interesting that isolations were not made from those obtained on admission, but that in all 5 specimens the viruses were recovered from stools taken three to nine days after admission. This suggests that the viruses were acquired by the patient during his stay in the hospital and were therefore better associated with this factor than with the clinical illness responsible for admission. The appearance of these agents in the stools was not accompanied by any unusual clinical manifestations. Clearly, then, the potential role of the hospital in the spread of these agents must be determined and, of course, considered in the evaluation of the etiologic significance of agents encountered during studies of hospital inpatients. This point takes on added importance when the unquestioned role of the household in the spread of Coxsackie viruses is appreciated.[23] Finally, it was interesting to note, during these extensive studies, the paucity of isolations of Coxsackie viruses from cases of clinical poliomyelitis in areas and at times when these viruses were extremely prevalent. Strange as it may seem, therefore, it is the extreme prevalence and ease of demonstration that has made it most difficult to assess the role of these viruses in human disease.

It should be unnecessary to emphasize the fact that controls are as essential in epidemiologic investigation as in laboratory experimentation. They have not, however, been used in most studies of Coxsackie viruses in human subjects; this is particularly unfortunate when the question is, as here, one of the possible etiologic roles of a newly discovered group of extremely prevalent viruses. It appears that many investigators consider causation of illness by a new organism to be adequately shown by isolation of the organism, or more than well demonstrated if a concurrent rise in homologous antibody is also shown. This combination, of course, provides good evidence that the patient was infected with the organism — but *it cannot, in the absence of epidemiologic studies including adequate controls, show that signs and symptoms that the patients may have at that time are necessarily due to that infection.* This is especially true when the signs and symptoms are protean, or resemble those of an already recognized disease and when, as in most studies of the occurrence of Coxsackie viruses, the patients have been selected on the very basis of possessing such signs and symptoms.

Criteria for Etiologic Associations

Obviously, the first question that must be answered concerning microbes found as often in association with health as with disease is the very basic one of whether or not such agents are pathogenic. This is a particularly pertinent question to ask since it can be shown that it is not only a theo-

*These studies were made possible through the co-operation of Drs. R. H. Parrott, S. Ross, F. G. Burke and E. C. Rice, of the Children's Hospital, Washington, D. C.

retical possibility but a nearly predictable certainty that, because of their ubiquity, such agents would occur by chance during any and all states of illness and well-being — particularly, however, in children in the summertime. Under such conditions the mere isolation of virus and the demonstration of antibodies from selected ill persons represent necessary, but in themselves inadequate, evidence for establishing etiologic relations. Methods for large-scale sampling for these viruses in human communities have been developed.[7] These methods, then, were applied to epidemiologic studies of the occurrence of illnesses and viruses in such groups. Intensive observations of normal populations in several parts of the country seem to have provided a sound basis for eventually discovering what some of these viruses are doing as human parasites. This is no more or less than acquiring answers to the very important question — "what do the controls show?" — before attempting to explain phenomena observed in test groups. By a study of outbreaks of illness and at the same time of many other persons who were not ill and who lived in the same area and were in all important respects equivalent, it was possible with these investigational methods to provide evidence that the Coxsackie viruses under natural conditions do indeed cause illness in man.

Herpangina

During studies in Parkwood, Maryland, and Woodmont, Virginia, communities and in Washington, D. C., hospitals in 1949 through 1951, it was found that a seldom recognized but widely prevalent childhood disease known as herpangina seemed to be the chief clinical manifestation of infection with many, if not most, of the so-called Group A Coxsackie viruses.[23, 24, 32]

Herpangina is a specific febrile disease of childhood that occurs usually in epidemic form in the summertime and is characterized by small to minute ulcerative lesions of the posterior parts of the mouth and the throat. It was first described as a distinct clinical entity by Zahorsky[81] in 1920. Other physicians, apparently unaware of Zahorsky's original report, described outbreaks of the same illness in a summer camp[75] and a nursery school.[82] The following is a brief clinical description of the disease given by Zahorsky[83]:

> The disease begins suddenly as an acute febrile movement. The temperature often rises to 104°. A convulsion may occur. Vomiting is often present. Anorexia and prostration are sometimes marked. The throat and posterior post of the mouth show minute vesicles, or if these have ruptured, small punched-out ulcers. They occur on the anterior pillar of the fauces, the tonsils, the pharynx and the edge of the soft palate. The number of the lesions varies from two to twenty. Dysphagia is often marked. The general and local symptoms disappear in a few days. The disease may be easily confused with ulcerative stomatitis which sometimes begins in the throat. The prognosis is favorable and the treatment is symptomatic.

Little can be added to this description of the clinical entity.[24, 84] The disease with which herpangina may be most readily confused is herpetic gingivostomatitis, especially when pharyngeal lesions occur in the latter, but it may readily be distinguished from other illnesses such as thrush, the various "aphthae" of allergic, traumatic or unknown origin, and the enanthemas of measles, varicella, scarlet fever and diphtheria.[84] Heavy metal intoxications, deficiency diseases and hematologic disorders may also cause oropharyngeal lesions. If, in a case of herpangina, pharyngeal lesions are missed or if typical lesions do not develop during observation (as has been observed in ill siblings of patients with definite cases),[85] a specific clinical diagnosis is virtually impossible since many other mild illnesses of childhood exhibit fever and the other less regularly observed symptoms of herpangina. However, the pharyngeal lesions are quite characteristic and when present can be regarded as pathognomonic evidence of the disease.

Our etiologic investigations of herpangina, which continued from 1949 through 1951, showed that the disease was associated with the presence of 1 of 6 Group A Coxsackie viruses in feces or throat secretions, or both, in 85 of 99 cases. In each of the separate studies, herpangina was shown to be associated with one or more of these 6 immunologic types of virus. It should be emphasized that while cases of herpangina were being studied for virus, suitable control groups consisting of household and neighborhood contacts, normal persons living in the same communities, and hospitalized and clinic patients with other diagnoses were examined concurrently for the presence of virus. The epidemiologic data based on virus isolations showed that viruses were most frequently recovered from patients (85 per cent), next often from their neighborhood (60 per cent) and familial (40 per cent) contacts and least often from all other categories (3.5 per cent).

A recent report of Kravis, Hummeler and Sigel[25] has described the isolation of Group A viruses from children ill with herpangina in Philadelphia in 1951. The predominant strain associated with the outbreak was the H3 type.

As mentioned above in the section on epidemiology, the isolation of the Group A viruses as reported by investigators in this country and abroad indicated that these viruses have worldwide distribution. It is not necessary, however, to stray more than a few miles from the doorstep of one's laboratory to be impressed by the ease with which these agents, most of which appear to cause herpangina, may be demonstrated in children during the summer months. Thus, in 1949, 4 different Group A viruses were found to be occurring almost simultaneously in Parkwood, the community nearest to the National Institutes of Health. Studies in 1950 in patients at Children's Hospital Clinic and those seen in private practice in the Washington area indicated that 6 types were occurring that

summer. In fact 1 person was shown to be harboring 2 Group A viruses simultaneously and different members of a household had 2 different types. Studies in Parkwood in two years showed that 5 persons ill with herpangina caused by Type 2 in 1949 harbored a different immunologic type (H3) in 1950, either as cases or as familial contacts of patients with herpangina.

Additional evidence for the widespread occurrence and distribution of these agents was acquired during serologic surveys performed in Parkwood in 1949 and 1950 concomitantly with the testing of fecal specimens for virus.[57] The total prevalence of neutralizing antibodies against 5 different herpangina viruses ranged from 43.5 to 80.2 per cent for any 1 virus, thus indicating widespread previous infections in the population studied. Analysis of the prevalence of these antibodies by age showed that a significantly higher percentage of adults than of children had antibodies against each virus type, and that adults tended to have antibodies against more virus types than children did. Other data, acquired by testing of serums collected before and after appearance of virus and illness in some members of households, aided in explaining the age distribution and the spread of infection and illness: the results of these serologic tests demonstrated that infection occurred only in persons without pre-existing, type-specific neutralizing antibodies, whereas persons with previous antibodies, but similarly exposed within the household did not become infected with the homotypic virus. This study confirmed the hypotheses that herpangina and Group A virus infections occur most frequently in the young and are probably spread by contact between them. It was further concluded that children become infected repeatedly when subsequently they are effectively exposed to different strains of virus so that as they become older they are immunized against many virus types. The frequency with which these infections cause clinically visible illness is undetermined. In our community studies the prevalent strains produced illness in 30 to 50 per cent of infected persons — suggesting that, compared to poliomyelitis viruses, some of the Group A strains produce characteristic illness with great frequency, and result in type-specific neutralizing antibodies that persist for at least one and probably many years. The conclusion seems warranted, therefore, on the basis of virus isolations performed in our own and other laboratories, and on the basis of serologic studies, that herpangina is one of the most frequent and widespread of the minor diseases of childhood.

Epidemic Pleurodynia

Curnen, Shaw and Melnick,[41] Weller et al.,[39] in New England, and Lazarus,[43] in Seattle, Washington, have described the occurrence of Group B Coxsackie viruses in persons with epidemic pleurodynia or "Bornholm disease." Again, these studies were retrospective studies confined to persons with disease. However, the demonstration at Yale[42] that laboratory infections with some of the B agents produced pleurodynia-like illnesses provided additional evidence for the hypothesis that these agents might be responsible for naturally occurring epidemic pleurodynia.

This alarming, but nonfatal, disease occurs both in epidemic and endemic forms and has recently been reported from various parts of the world in ever-increasing numbers. It is characterized by sudden onset of abdominal or chest pain, fever, headache and anorexia, with associated respiratory distress. Invariably, all patients recover, but relapses and complications occur, and convalescence may be prolonged. The clinical diagnosis of this disease in the sporadic suspected case, however, is difficult if not impossible. Appendicitis, commonduct obstruction, pancreatitis, coronary occlusion, pneumonia, pleurisy and intestinal infections are only a few of the diseases that may readily be simulated by epidemic pleurodynia. However, the spatial and temporal relations between illnesses occurring during outbreaks of the disease in rural areas as described by Pickles,[86] Sylvest[87] and others[88, 89] reveal a stereotyped pattern that is easily recognized.

An opportunity was provided representatives of the National Microbiological Institute in 1951 to assist local health authorities in an investigation of an outbreak of epidemic pleurodynia in the northeastern part of Texas. The outbreak provided a unique opportunity to perform laboratory studies of this disease contemporary with its actual occurrence in the general population. Here, again, attempts were made to study large areas and to include large groups of normal persons who had no signs of the disease.[36, 59]

It was disturbing but not surprising to find immediately that Group A viruses could readily be isolated from the feces of a few persons with epidemic pleurodynia. A noncritical and superficial investigation could well have closed with these findings on cases alone and would have presented what would certainly have been an entirely false picture of the true state of affairs. Intensive investigations of other sick persons and of healthy subjects revealed that a Group A virus was indeed prevalent in the area where a great deal of epidemic pleurodynia was also occurring. However, and this is most important, the virus was not found in any of the cases of pleurodynia occurring in a nearby small community placed under intensive study. Most of the patients were found to have another virus — a Group B type that had previously been isolated by Lazarus from several patients with epidemic pleurodynia in Seattle, Washington. Furthermore, it could be shown that the sick persons from whom the Group A virus had been isolated

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earlier also contained in their feces the same Group B virus, which because of its slower development in the suckling mouse had not at first been recognized. Although all the data from this study have not yet been analyzed, at least two important points seem to be clear: there is no substitute for intensively controlled observations on the occurrence of prevalent infectious agents in the human population, any more than there can be substitutes for controlled experiments in the laboratory; and present evidence appears to support the hypothesis that epidemic pleurodynia is caused by one or more Group B Coxsackie viruses.

Simultaneous Occurrence of Viruses

One of the more interesting questions to be considered is that of simultaneous infection by two or more of these extremely prevalent Coxsackie viruses, or by these viruses together with the almost equally prevalent poliomyelitis viruses. Although current knowledge explains adequately what many of these viruses may do when they occur alone, there is no clear-cut information concerning their behavior when they occur together in a single human host. The question of whether accentuated disease would be produced[33, 34, 80] or whether interference would result in less manifest disease[90, 91] must still be answered. Certainly, the reports of at least 50 different cases of such combined infections, which point out the high probability that such prevalent agents occasionally occur together, make this question a pertinent one in the virus field today.

Summary

It is apparent that Coxsackie viruses are among the most recently recognized agents of disease, and that physically and epidemiologically — though not pathogenetically nor immunologically — they resemble the viruses of poliomyelitis and may therefore occur with them under the same conditions — even in the same human host. They are among the most prevalent of recognized viruses; although they have not been found to cause death in human beings, they cause considerable misery and distress, and are therefore of clinical as well as theoretical importance. The roles of all these viruses have not been determined, but controlled studies have indicated that many of those known at present cause either herpangina or epidemic pleurodynia; there is no good evidence at present that they influence, in mixed infections, the course of poliomyelitis. However, the significance of mixed infections requires more study. Beginning in early childhood inapparent and missed infections with different types of Coxsackie viruses occur repeatedly; this very prevalence has forced a critical scrutiny of the criteria customarily used to establish the etiologic significance of human viral parasites, and has necessitated new concepts of the viral "flora" of man. The comparative ease with which these agents can be isolated and handled in the laboratory provides an excellent opportunity for studying the basic nature of small viruses, new methods of mass sampling for viruses and the epidemiology of viruses transmitted by similar routes.

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Correction. In the first and fifth paragraphs of the case report in the paper entitled "Abdominal Pregnancy Secondary to Rupture of Accessory Uterus with Survival of Mother and Infant," by Drs. George A. Bourgeois and Morris W. Shapiro, which appeared in the July 17 issue of the *Journal*, the sentences beginning "Laboratory examination revealed" should be changed to read, respectively "Laboratory examination revealed a red-cell count of 3,130,000, a hemoglobin of 60 per cent and a white-cell count of 13,700," and "Laboratory examination revealed a red-cell count of 3,320,000, a hemoglobin of 60 per cent, a white-cell count of 14,400, with 81 per cent neutrophils, and an essentially normal urine."

MEDICAL INTELLIGENCE

THE CARDIAC WORK CLASSIFICATION UNIT

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BOSTON

TO MANY the term "Work Classification Unit" may convey little of significance. Since such a unit is shortly to be opened, however, under the combined aegis of the Massachusetts Heart Association, the Bay State Medical Rehabilitation Clinic, the Massachusetts General Hospital, the Massachusetts Department of Public Health and the Division of Vocational Rehabilitation of the Department of Education, it seems proper that an explanation of its purposes and methods should be set forth to the medical profession.

HISTORICAL BACKGROUND

For some years much has been said, but relatively little has been accomplished, regarding the problem of fitting the partially handicapped cardiac patient into his proper place of employment in industry. It has been realized increasingly that far too many cardiac patients have been shelved, often through the fears of relatives or employers and even through fears of their physicians, when they actually have many years of potentially useful service to themselves and their families before them. Many of these fears were grounded upon the fact that no one was quite certain what the potentialities of these patients were. In 1940 the New York State Employment Service approached the New York Heart Association with a request for help in attempting to solve certain of these problems relative to job placement. As a result the first work-classification unit was established under the leadership of Dr. Leonard J. Goldwater in 1941 as a part of the Adult Cardiac Clinic, Bellevue Hospital, New York. For more than ten years this clinic has functioned successfully and has established methods and data relative to this problem. World War II served as a great stimulus in demonstrating clearly, with the shortage of workers, that many persons with cardiac disease, if properly evaluated and placed, could carry on successfully with a wide range of occupations. In April of 1949 a work-classification unit was opened in Cleveland under the auspices of the Cleveland Heart Society. This clinic has continued to grow and has filled successfully a need much felt in the community. The American Heart Association has been sufficiently impressed by the past work of these clinics and that of several others that have since come into being to prepare a manual for "The Work Classification Unit" and is fostering the extension of such facilities by other communities throughout the country.

The Massachusetts Heart Association, through its Committee on the Cardiac in Industry, has contemplated the establishment of a work-classification unit for some time. The opening of the Bay State Medical Rehabilitation Clinic, located within the ground of the Massachusetts General Hospital, seemed to offer an ideal location and setup for such a clinic. By the co-operation of these two organizations, together with assistance from the Massachusetts Department of Public Health and the Division of Vocational Rehabilitation of the Massachusetts Department of Education, plans have now been consolidated for the opening of the Work Classification Unit this September. Additional space in the Bay State Rehabilitation Building has been provided.

PURPOSE

The primary purpose of the Work Classification Unit is to furnish a consulting service to private physicians, clinics, industries, public and private agencies, insurance companies and other interested organizations in the matter of cardiac diagnosis and classification of persons in relation to their capacities for specific employment in industry. This may take the form of recommendations for special placement of those already employed. On the other hand it may evaluate the potentialities of a patient with recognized cardiac disease for vocational-rehabilitation training under the Massachusetts Department of Education. Again, it may recommend suitable placement of unemployed cardiac patients with the assistance of vocational counseling and social service.

The second purpose of the clinic is to carry on and foster further research in the entire field of physical fitness for various types of work in industry from the clinical and laboratory point of view with an aim of evaluating further the available tests of physical capacity, and to develop, if possible, more satisfactory criteria for types of suitable occupation. Also, it is of importance to observe the effect of various occupations on the cardiac patient.

The third purpose is to further the education of all concerned, especially physicians and industrialists, regarding the possible and proper utilization

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of workers with various cardiac handicaps in industry. Above all, it is essential that knowledge of optimum use of facilities now available for rehabilitation through various agencies be disseminated. The development of a social consciousness of the true meaning of rehabilitation and its economic connotations, with the removal of safely employable persons from public-welfare rolls, is of great value. The correlation of this work with the attitudes of insurance companies, laws regarding workmen's compensation and opinions of labor unions will be all important.

Finally, this project represents an endeavor that is relatively in its infancy, and it is hoped that the clinic will serve as one of the pilot studies for the development of similar units.

Eligibility

Although it is anticipated that this clinic will primarily serve the metropolitan Boston area, its facilities will be available to any person living in Massachusetts who is desirous of cardiac evaluation for employment. Referral in writing will be required from a physician, hospital clinic or social agency, preferably giving the patient's medical history. Financial status will not effect eligibility.

Financial Responsibility

Referring agencies, private industry and insurance companies will be expected to stand the cost of the patients' evaluation when possible. These persons will be expected to pay whatever part of the expense they are able to meet either at the time of evaluation or subsequent to obtaining employment. The Massachusetts Heart Association has agreed to underwrite the initial financial support of this project, and the Bay State Rehabilitation Center is furnishing clinic space and administration.

Methods

It may be stated that the key to proper carrying out of this project is co-operative teamwork on the part of numerous specialists. It may well be asked why any cardiac clinic cannot assume the project as proposed. The answer to this is that the average cardiac clinic finds its time spent at present in the fields of diagnosis, therapy and teaching and has neither the time nor the varied personnel required for detailed occupational tolerance classification. Concentration on this special aspect has up to the present brought forth results not obtained otherwise. The teamwork required precludes the possibility that any individual physician can accomplish this purpose.

Patients will be seen by appointment at the clinic sessions on Thursday evenings. A complete and detailed history and physical examination, with emphasis on the cardiovascular system, will be made by an internist and a cardiologist. Routine laboratory studies will include serologic tests, urinalysis, hemoglobin and blood counts or other studies as indicated, electrocardiograms, exercise-tolerance tests as warranted, ballistocardiograms, fluoroscopic study in co-operation with the X-Ray Department of the Massachusetts General Hospital and x-ray films as indicated. Other special tests such as oxygen consumption may subsequently be done. All patients will be interviewed by a medical social worker with special inquiry into problems of family needs, insurance, financial support and factors of work motivation that have proved all important. Then there will be an interview with a vocational counselor regarding past work experience and potentialities. Finally, with the above data assembled, all those who have examined and interviewed the patient will join in a round-table discussion to summarize the case and make recommendations. Family physicians, industrial physicians or others interested will be invited to be present to enter into these conferences with the objective of reaching the optimum decisions for the patient and for further education of all concerned.

After this a detailed written report with findings and recommendations will be forwarded to referring physicians and agencies. In all cases, regardless of the source of referral, a copy of the report will be sent to the family physician. Although the clinic itself cannot function as an employment agency, the social worker and vocational counselor will follow through, making contacts for the patient with his former employer, the Division of Vocational Rehabilitation or, when necessary, other agencies for employment.

The clinic will request follow-up visits at stated intervals to give an opportunity of observing how recommendations have worked out and also to study the effect of employment on the patient. In some cases later reclassification may be required.

In certain cases it may be suggested that the patient return to the Rehabilitation Clinic to carry out trial periods of work under supervision in the occupational-training department either to establish confidence or to test work capacities further.

In no case will any treatment, other than occupational therapy or informal psychotherapy, be carried out. Estimation will be made concerning whether optimum therapy is underway and suggestions, if any, for changes in treatment will be made only to the referring physician or clinic.

Relation to Family Physicians

The reaction of some doctors may be that this is another clinic to encroach upon their rights and relations with patients. When the nature of the clinic and its methods are understood this should present no problem. The unit should offer a helping hand to the physician in carrying out an important mission to certain patients that no doctor

alone could well undertake. Actually, in Cleveland some 60 per cent of the patients have been referred by private physicians who have accepted the clinic as a most helpful adjunct. Indeed, it seems likely that return visits to family physicians may actually be stimulated and increased by suggestion and advice of the clinic. The rule of no direct therapeutic instructions to patients will be strictly adhered to, and this matter will remain in the family doctor's hands. In referrals from industry, the family physician will also receive reports and recommendations.

Clinic Opening and Appointments

Details regarding these matters will appear subsequently in the *Journal*.

Summary

A work-classification unit for evaluation of the cardiac patient regarding proper employment will be opened shortly in Boston. The historical background, purpose and methods of the unit are outlined.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38341

Presentation of Case

A fifty-six-year-old man was admitted to the hospital because of pain and stiffness of multiple joints.

Eight weeks prior to admission the patient noted pain, stiffness and some limitation of motion in the shoulder joints. Pain and stiffness in the ankles, knees and fingers subsequently developed; the left ankle only became swollen and tender. Coincidental with the onset of the joint symptoms he noted redness and lacrimation of both eyes; he was treated with cortisone drops, with only slight relief. The symptoms varied in severity during the subsequent two months but were always present. For a few weeks prior to admission he had been anorexic, and he believed that he had lost some weight. He had had occasional chills and fairly marked malaise, but no known fever. There was no history of urethral discharge, gout or skin rashes.

Three months prior to entry he had an attack of "pleurisy." Nine years before admission he had been in the hospital because of renal colic on the right and had passed a calculus from the right ureter spontaneously; on examination at that time the blood pressure was 120 systolic, 80 diastolic, the nonprotein nitrogen was 28 mg. per 100 cc., and the urine had a specific gravity of 1.025 and showed no significant findings.

Physical examination revealed a well developed man in no acute distress. There was a bilateral conjunctivitis, some haziness of the right cornea and a low-grade iritis. The heart, lungs and abdomen were normal. There was some limitation of movement of the shoulder joint, most marked on the left. The left ankle was swollen and slightly warm, but there was no definite evidence of involvement of any other joints.

The temperature was 99°F., the pulse 80, and the respirations 20. The blood pressure was 120 systolic, 70 diastolic.

The urine had a specific gravity of 1.014 and gave a ++ reaction for albumin; the sediment contained 20 red cells, 10 white cells and frequent granular and hyaline casts per high-power field. Culture of the urine showed no growth. Examination of the blood revealed a hemoglobin of 12.4 gm. and a white-cell count of 11,200, with 76 per cent neutrophils, 10 per cent lymphocytes, 7 per cent monocytes and 7 per cent eosinophils; the platelets and red cells appeared to be normal on examination of a blood smear. The sedimentation rate was 20 mm. in fifteen minutes and 60 mm. in one hour. Examination of a smear for "L.E" (lupus-erythematosus) cells was negative. The nonprotein nitrogen was 70 mg., the uric acid 4 mg., the protein 5.54 gm., the albumin 3.64 gm., and the globulin 1.9 gm. per 100 cc. Numerous blood cultures showed no growth. An agglutinin test for Brucella was negative. A roentgenogram of the chest demonstrated emphysematous lungs, pleural thickening at the right costophrenic sulcus, several linear streaks in the region of the right middle lobe and some enlargement of the heart. A gastrointestinal series was normal. X-ray films of the left ankle showed a fair amount of soft-tissue swelling and moderate osteo-

porosis; the joint surfaces were smooth and the joint spacing intact. An electrocardiogram was normal.

During the entire hospital stay, the patient continued to have marked weakness, was anorexic, had migratory joint pains and had an elevated temperature ranging from 99 to 102°F. The urine consistently gave a ++ to +++ reaction for albumin, and the sediment contained numerous red cells and varying numbers of granular and hyaline casts. The hemoglobin gradually fell to 10.2 gm. and then to 8.2 gm. in spite of blood transfusions. The lesions in the eyes gradually improved after treatment with cortisone eyedrops. He was given terramycin, without definite improvement, from the fifth to the tenth day; the drug was discontinued because of nausea. Because of anorexia and nausea he was given supplemental intravenous feeding during the entire stay.

On the seventeenth day severe pleuritic pain in the left lower portion of the chest developed, and two days later he coughed up dark-red blood; tenderness was noted in the left calf. X-ray examination of the chest revealed a small patch of density at the left base; an electrocardiogram showed that in comparison to previous tracings the rate had increased and the T waves were slightly lower, particularly in Leads 3, AVF, V_4, V_5 and V_6; the white-cell count was 17,700, with 88 per cent neutrophils, the nonprotein nitrogen 97 mg. per 100 cc., the serum potassium 5.6 milliequiv., and the carbon dioxide 17.8 milliequiv. per liter; the serum sodium and chloride were normal. A bilateral common-femoral-vein ligation was carried out; no clots were found at the level of the operation.

For the week after this he received penicillin, but then a macular morbilliform rash developed and the drug had to be stopped on the twenty-sixth day. On the following day he passed a grossly bloody stool and vomited a small amount of blood-streaked material; the nonprotein nitrogen was 140 mg. per 100 cc., the serum sodium 133.5 milliequiv. and the chloride 98 milliequiv. per liter, and the prothrombin time 16 seconds (normal, 14 seconds). He next received cortisone intramuscularly for four days; the rash faded, and he ate better and felt better generally, but the urinary output dropped and he became very nervous; the drug was discontinued. On the thirty-fifth day sacral edema developed and pulmonary rales were noted, and later in the day he complained of a nonradiating lower substernal ache accompanied by dyspnea; examination showed moist rales in the lung, normal heart sounds and a blood pressure of 168 systolic, 70 diastolic. An electrocardiogram revealed sinus tachycardia at a rate of 110, a PR interval of 0.12 second; the T waves were low in Leads 1, 2, 3, V_1, V_3, V_4 and V_6, and upright in V_2; the ST segments were sagging in Leads V_2 through V_6. The nonprotein nitrogen was 150 mg., the calcium 7.3 mg., and the phosphorus 9.1 mg. per 100 cc.; the sodium was 122.7 milliequiv., and the carbon dioxide 18.9 milliequiv. per liter. The white-cell count was 10,600, with 88 per cent neutrophils. The urinary output progressively decreased, and the nonprotein nitrogen rose to 265 mg. per 100 cc. The patient became progressively weaker, continued to have rales in the chest, became semicomatose and died quietly on the fifty-fourth day.

Differential Diagnosis

Dr. William S. Clark*: In summary this fifty-six-year-old man entered the hospital eight weeks after the onset of polyarticular joint disease associated with chills, anorexia, weight loss and iritis. While he was in the hospital, a pulmonary infarct, a sensitivity reaction to penicillin, gastrointestinal bleeding and, after the administration of cortisone, fluid retention and congestive failure developed. There was gradually progressive renal disease, with an increase in blood pressure, nonprotein nitrogen and serum phosphorus and a decrease in serum calcium, followed by death in uremia. There was no evidence of infection as the cause of the disease. The renal stone that he had had years before entry seems unrelated.

The evidence that several systems were involved, including the kidneys, the joints, the eyes and subsequently the heart, seems to put that illness into the general category of what is referred to as connective-tissue diseases, collagen diseases, rheumatic diseases or more recently "group disease." These terms denote the inflammatory diseases of unknown etiology in which many systems are involved, usually with some form of arthritis. Most of these diseases can be classified into separate entities by certain characteristics: rheumatoid arthritis by the nature of the joint involvement; disseminated lupus by the skin, serous-membrane and renal involvement; dermatomyositis by the predominance of muscle involvement; scleroderma by the hardening of the skin; and rheumatic fever by the character of the heart and joint disease. In addition, there is a poorly circumscribed group that we refer to by the term polyarteritis nodosa. Over the past several years, beginning with a case discussed by Dr. Rackemann,[1] we have observed a highly bizarre group of patients with the label polyarteritis nodosa who have widespread vascular involvement sometimes with vascular and extravascular granulomas and frequently with overlapping characteristics of other members of this group. In spite of the variety of names and labels that have been applied to this whole group of disease, I think it is generally recognized that they all have some form of vascular involvement varying from minimal perivascular collections of lymphocytes to the more florid types with necrotic panarteritis and granuloma formation.

Without more discussion, I am going to place this patient in the category of diffuse vascular disease that we have been labeling polyarteritis nodosa.

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In our experience, eye involvement in this particular entity has not been a common finding, but more and more we are learning that we cannot depend upon such experience because each year brings new cases of overlapping of one entity with another. Because of the nature of joint involvement, the pronounced renal disease and the presence of eye involvement, I shall choose that particular type of polyarteritis nodosa in which diffuse granulomas are demonstrated. I cited Dr. Rackemann's case because that particular experience first called to our attention the generalized granulomatous disease associated with polyarteritis. The experience, however, that influences me the most in putting it into the granulomatous group is the case that Dr. Lerman[2] discussed two years ago. That patient also had widespread systemic inflammatory disease and died in uremia. I am not implying, however, that death in uremia indicates granulomas in addition to vascular necrosis.

It is interesting that at that time Dr. Tracy B. Mallory applied the name Wegener's granulomatosis to Dr. Lerman's case, in which there was widespread panarteritis with multiple granulomas, foci of necrosis and giant cells. He stated that the disease had originally been described in connection with the lung in 1936[3] and 1939.[4] I have the opinion that all these cases have something in common. When Dr. Paul Klemperer visited us a few years ago, we mentioned Dr. Rackemann's case and he said that he had had similar cases to which he had applied the term allergic granuloma. The relation of these lesions is a problem that we never get into the middle of; we are always at the periphery. In the general group of connective-tissue disease, there are certain entities that we can classify even to the point of prognosticating, but there is also a large group that we cannot classify. In this residual group there is a group in which the characteristic feature is a diffuse necrotizing arteritis. In addition to the more classic form of necrotizing arteritis, granulomas have been observed that resemble in many cases the granulomas described in other members of the group, particularly rheumatoid arthritis and rheumatic fever.

I choose polyarteritis nodosa as the most likely diagnosis to explain this course, including the pulmonary, eye, heart and renal involvement. I shall go one step farther on the basis of Dr. Lerman's experience and state that it was probably of the granulomatous type, such as Wegener's granuloma or Klemperer's allergic granuloma.

Dr. J. Wallace Zeller: Did Dr. Clark rule out lupus erythematosus?

Dr. Clark: The patient had many of the characteristics and could have had disseminated lupus erythematosus. The clinical feature against it was the leukocytosis during a period of exacerbation of the disease in the absence of infection. The one negative lupus-erythematosus-cell preparation certainly would not rule it out; we have found no "L.E." cells on several occasions in such cases. It does not matter to me whether one calls this disseminated lupus erythematosus or what one calls it — the basic lesion is a widespread vascular disease.

Dr. Benjamin Castleman: Dr. Bauer, have you any comment?

Dr. Walter Bauer: I saw this patient a day or so before he died and thought the clinical course was more consistent with what we usually term polyarteritis nodosa.

Dr. Castleman: Dr. Lerman, was this case similar to yours?

Dr. Jacob Lerman: It certainly sounds like it.

Dr. Bauer: The patient that Dr. Lerman discussed had been sick for about seven years and for a long time had nothing to show except the joint involvement and slowly progressive arterial disease.

Dr. Zeller: That patient also had amyloid disease and chronic nephrosclerosis.

Dr. Arthur S. Pier, Jr.: Would you consider amyloid disease here?

Dr. Clark: Ordinarily with arthritis, amyloid disease involving the kidney is of the secondary type. I do not believe the arthritis had been present in this patient long enough to cause amyloidosis. Primary amyloidosis usually does not produce this type of renal involvement.

Clinical Diagnoses

Polyarteritis nodosa.
Uremia.

Dr. Clark's Diagnosis

Polyarteritis nodosa, granulomatous type.

Anatomical Diagnoses

Polyarteritis nodosa involving kidneys, intestine, testicle and periadrenal fat.
Myocarditis, acute.
(Uremia.)
Pleuritis, fibrinous, bilateral, severe.

Pathological Discussion

Dr. Castleman: This patient had a disease that we called polyarteritis nodosa; perhaps it should have been called a vasculitis because not only arteries but also veins in some places were involved. It was not, however, as generalized a disease as we expected to find; the spleen, the liver and the adrenal glands were not involved. In the periadrenal fat there were several large arteries that showed the classic picture of polyarteritis nodosa — that is, fibrinoid necrosis in their walls, and secondary thrombosis — a very acute fulminating type of arteritis.

In the small bowel we found several black dots scattered along the serosa; these proved to be serosal thrombosed veins whose walls in many places were necrotic. There were also small petechial hemor-

rhages of the mucosal surface close to these lesions. The testis showed small lesions in the vessels, whose walls were so necrotic that we could not tell whether they were veins or arteries.

The heart muscle demonstrated an extensive myocarditis, with necrosis of the muscle fibers and polymorphonuclear infiltration; we could not find even a small artery that was involved with arteritis, or any form of vasculitis; the major vessels did not show any lesion.

The kidneys in the gross contained large numbers of petechial hemorrhages, such as we often see in polyarteritis nodosa. The microscopical sections, considered alone, presented a classic picture of chronic glomerulonephritis: beautiful adhesions of the tufts, crescent formation, organization of the capsule and fibrosis consistent with a healing state of chronic glomerulonephritis. In some of the tufts we found evidence of acute necrotizing glomerulitis; there were no arterial changes. We have found similar necrotizing changes in other cases of polyarteritis nodosa. Thus, these vascular changes involved the capillaries rather than the larger vessels of the kidney, and the process had continued long enough to organize and to produce an appearance that can be called chronic glomerulitis.

None of the sections showed a granulomatous reaction that could be called the allergic form of vasculitis; of course, the whole condition may be an allergic reaction.

DR. CLARK: The only observation close to it would be the extravascular lesions in the myocardium, which we have observed in 2 patients.

DR. CASTLEMAN: Grossly, all the serous surfaces — pleura, pericardium and peritoneum — showed an acute fibrinous process such as is often seen in cases of lupus erythematosus.

DR. CLARK: My only point in emphasizing the granulomatous nature is to bring out the fact that these patients can have extravascular lesions and that one cannot always explain clinical findings on the basis of previous experience with vascular occlusions and infarctions.

DR. CASTLEMAN: The only extravascular changes were in the heart. The lungs showed a pneumonic process, but no vascular changes. We would not put this case into the class of Wegener's granuloma.

DR. CLARK: I really do not approve of the terminology; I think it only confuses us more if unusual forms of polyarteritis are given eponyms.

Did you have the opportunity to examine the eyes?

DR. CASTLEMAN: No.

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CASE 38342

PRESENTATION OF CASE

A twenty-five-year-old man was admitted to the hospital because of a chronic cough.

Three months before admission the patient developed a cough productive of yellowish sputum, which was occasionally blood streaked and which occasionally induced vomiting, most often in the evening several hours after meals. After treatment with penicillin, the cough was somewhat less troublesome. Seven weeks before admission he developed a "cold," with coryza and accentuation of the cough. The following week the cough became more severe, and he developed anorexia, chills, night sweats and a fever — maximum temperature of 103 to 104°F. Thereafter, usually at night in bed, he had severe coughing paroxysms during which he vomited white phlegm. He coughed up a quarter cupful of bright-red, partially clotted blood one night and had blood-streaked sputum on two other occasions. He was treated with injections and "yellow capsules," but the symptoms persisted; he was unable to eat because of the cough and vomiting and lost 20 pounds in weight in three weeks. Twelve days before admission he entered another hospital, from which after eight days he signed himself out. At home the cough, sputum, vomiting, anorexia and night sweats continued unchanged.

There had been no serious illnesses in the past; a right herniorrhaphy and appendectomy had been performed five years before admission. There was no known exposure to tuberculosis. For four months prior to entry the patient had periodic, fleeting dizzy spells, lasting only a few seconds and not accompanied by loss of balance or consciousness. In the two months prior to entry he had noted some shortness of breath on exertion, but no orthopnea, paroxysmal nocturnal dyspnea or chest pain.

Physical examination revealed a well nourished man who coughed frequently during the examination but who was in no acute distress. There were no palpable cervical or supraclavicular lymph nodes. The chest expanded well and equally bilaterally. There was dullness to percussion, absent breath sounds and decreased tactile fremitus over the right posterior portion of the chest. The remainder of the physical examination was noncontributory.

The temperature was 98°F., the pulse 84, and the respirations 22. The blood pressure was 110 systolic, 70 diastolic.

The urine had a specific gravity of 1.015 and was normal. Examination of the blood showed a hemoglobin of 13 gm. and a white-cell count of 17,300, with 83 per cent neutrophils. The nonprotein nitrogen was 22 mg., and the total protein 6.7 gm. per 100 cc. A 1:100 dilution tuberculin skin test was negative. The sputum was thin and watery and contained a few small purulent flecks; examination

of smears of the sputum showed several gram-positive organisms but no acid-fast bacilli. Culture of the sputum grew out abundant alpha hemolytic streptococci, moderate *Neisseria catarrhalis* and a few diphtheroids. Roentgenograms of the chest showed a diffuse homogeneous density involving the entire right lower lobe, with considerable collapse of this lobe and a suggestion of a mass at the right hilus (Fig. 1). Fluoroscopic examination showed the diaphragm to move well bilaterally and no appreciable mediastinal shift. There was a suggestion of enlarged bifurcation nodes and on one spot film there was some indentation of the esophagus below the carina.

On the third day a bronchoscopic examination was performed.

Differential Diagnosis

Dr. Arthur S. Pier, Jr.*: Before beginning the discussion, may I look at the x-ray films?

Dr. Stanley M. Wyman: This very interesting set of films shows collapse of the right lower lobe (Fig. 1). The superior segment cannot be well out-

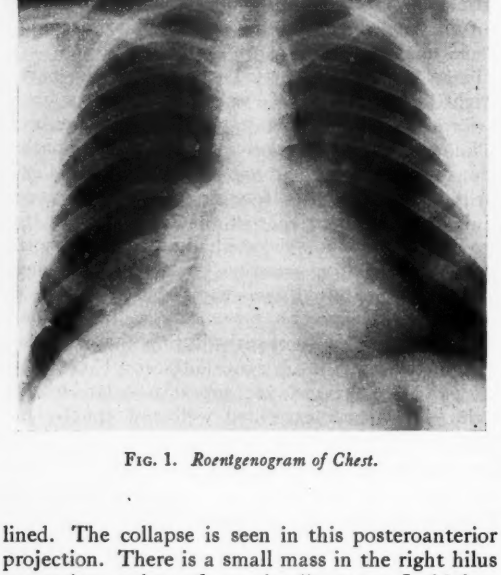

Fig. 1. *Roentgenogram of Chest.*

lined. The collapse is seen in this posteroanterior projection. There is a small mass in the right hilus measuring perhaps 3 cm. in diameter. I think a question would arise regarding what it represents. In the major bronchi, which can be traced fairly well, I do not see any definite abnormality. The indentation of the esophagus below the carina recorded in the protocol cannot be seen on these films. The film that showed that is missing.

Dr. Pier: You do not see any evidence of a foreign body?

*Assistant in medicine, Massachusetts General Hospital.

Dr. Wyman: There is no evidence of an opaque foreign body. I might say the right lower lobe is quite homogeneously dense. There is really no air in the bronchi of the lower lobe.

Dr. Pier: Can you trace the right-lower-lobe bronchus?

Dr. Wyman: Fairly well, down to the general vicinity of the mass described.

Dr. Pier: I find it somewhat difficult to fit any of the diagnoses one ordinarily thinks of into this picture because there are certain points against them all. One wonders whether these symptoms in a man of twenty-five years that were said to develop very suddenly three months before admission may not have been more insidious in onset. One also wonders whether the symptoms led to a wheeze at that time. As no wheeze was described, he presumably had none. Moreover one wonders whether he had any clubbing; that too was not described, and I therefore assume that he had none.

In a young man with cough and hemoptysis one thinks of tuberculosis, but tuberculosis is almost entirely ruled out. The x-ray picture does not suggest it at all; the tuberculin test was negative in a dilution of 1:100; and acid-fast bacilli were not found in the sputum, and certainly should have been found if he had endobronchial tuberculosis.

Bronchiectasis is a common cause of hemoptysis in young persons with cough. The patient probably had some bronchiectasis, localized and secondary to bronchial obstruction. I think one can say that he had definite evidence of bronchial obstruction, probably relatively complete, and that this bronchial obstruction was partly, at least, due to an intrabronchial mass because he had had bleeding. The bleeding may have been due to bronchiectasis and the obstruction may have been extrabronchial, but it seems to me more likely that he had an intrabronchial lesion.

Among the various causes of intrabronchial obstruction is bronchogenic carcinoma. The points in favor of bronchogenic carcinoma here are the rapid three-month course, with a rather steady downhill course, although he had received some benefit from antibiotics, and the bleeding, especially the streaky intermittent bleeding that he had from time to time. There are certain definite points against a carcinoma. He was extremely young for a bronchogenic carcinoma. There is no real confirmatory sign of carcinoma here. Both leaves of the diaphragm moved well bilaterally. A carcinoma causing so large a mass and so large an obstruction as this would probably cause some fixation of the diaphragm, at least on the right. There should also be clinical evidence of mediastinal involvement with a malignant tumor of this large size. I think, however, that carcinoma in spite of the age and in spite of these other factors has to be strongly considered. Incidentally he had no sign of metastatic carcinoma anywhere.

The physical examination was described as being negative except for the chest findings.

Other malignant lesions like lymphoma are extremely unlikely. I do not think a lymphoma would cause this much bleeding. There was no sign of lymphoma elsewhere in the body. The smooth mass in the x-ray films is consistent with a lymphomatous shadow, but I should be surprised if he had so much bronchial bleeding from a lymphoma, and I should expect more mediastinal manifestations.

Then the question arises of a so-called benign growth in the bronchus — a bronchial adenoma. I might say that in the recent literature[1] there is much skepticism about how benign these so-called growths are. Adenomas may extend through the bronchial wall, infiltrating and occasionally invading regional lymph nodes; a few cases have been reported in which there were distant metastases. Certainly, this patient's age makes one think of adenoma. His episode of bleeding of a quarter of a cupful of blood is characteristic of adenomas, which are inclined to bleed suddenly and to stop bleeding suddenly. The bronchial obstruction and pulmonary infection secondary to it would fit the picture of adenoma very well. The x-ray picture looks like adenoma. Against an adenoma are the rapidity of the course and the suddenness of the onset. Adenomas have usually caused symptoms for a long time before they are first diagnosed. It would be most unusual for an adenomatous mass of this large size to have caused symptoms for only three months. Commonly, a patient with an adenoma gives a history of intermittent bouts of pneumonia and intermittent bleeding long before the diagnosis is made. In one series of cases reported[2] the diagnosis was made anywhere from two to two and a half years or longer after the onset of symptoms. In the literature, I did not find any case that was diagnosed within six months of the onset of symptoms. If this was a case of adenoma, it was an unprecedented case of early diagnosis. The blood streaking of the sputum is unusual for adenoma and is more suggestive of carcinoma. In spite of these objections, I think adenoma is a strong possibility.

The third condition that is always an important consideration, when a patient suddenly develops purulent sputum, cough and bronchial obstruction, is a foreign body in the bronchus. Foreign bodies can sometimes be aspirated unconsciously or without any violent symptoms at the onset and then rather suddenly give rise to signs of bronchial obstruction and pulmonary infection. As I read through the history again, it seems to me that a foreign body in the right-lower-lobe bronchus is a not unlikely possibility. The process was on the right side, and most aspirated foreign bodies end up in the right lung. The sudden onset of purulent sputum would fit this diagnosis better than anything else. The x-ray picture, however, is very much against an aspirated foreign body. There was a definite mass, which I think is hardly consistent with a small foreign body in the bronchus, unless the mass represents an inflammatory reaction in the hilar lymph nodes secondary to pulmonary infection. I cannot see any evidence of a metallic foreign body in the bronchus. The patient may have aspirated a peanut, which I think would be the most common object for an adult to aspirate. Almost all foreign bodies are found in small children, and very few in adults of this age.

In summary, I shall bet against the diagnosis of adenoma because I think the onset was too sudden, the streaking of blood too atypical and the course too rapid. The diagnosis lies between carcinoma and a foreign body with an inflammatory reaction in the lymph nodes secondary to pulmonary infection. I am tempted on the basis of the x-ray picture to place carcinoma first on the list.

My diagnostic procedures would consist of a cytologic study of the sputum, in which one would expect to find malignant cells if carcinoma were present. Bronchoscopy, of course, is the court of last resort.

Clinical Diagnoses

Atelectasis, right lower lobe.
?Carcinoma.

Dr. Pier's Diagnosis

Carcinoma of bronchus.
?Aspirated foreign body.

Anatomical Diagnoses

Adenoma, right-lower-lobe bronchus.
Chronic pneumonitis, right lower lobe.

Pathological Discussion

Dr. Robert E. Scully: Dr. Benedict, who bronchoscoped this patient, will tell us his findings.

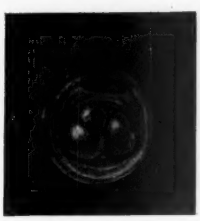

Fig. 2. *Smooth, Reddish, Lobulated Adenoma, Completely Obstructing the Right-Lower-Lobe Bronchus.*
The middle-lobe orifice is seen anteriorly at 12 o'clock.
(Reproduced from Benedict,[3] with the permission of the publishers.)

Dr. Edward B. Benedict: We found a smooth, gray tumor mass in the bronchus completely blocking the right-lower-lobe bronchus. The mass reached to the level of the middle-lobe orifice. We took a biopsy, which showed a benign bronchial adenoma.

I thought it would be interesting for you to see how these tumors look through the bronchoscope. This smooth, lobulated tumor (Fig. 2) is a good deal like the one we are discussing. The tumor in the case under discussion came closer to the margin of the middle-lobe bronchus than is shown in this drawing so that I thought the surgeons would have to remove both the lower and middle lobes to include the entire mass. This is another smooth gray adenoma blocking the left-lower-lobe bronchus, without left-upper-lobe obstruction (Fig. 3). The location of these tumors can be quite well shown by bronchoscopy, which helps the surgeon in determining his approach. The next slide (not illustrated) shows a lobulated tumor of the left-lower-lobe bronchus completely obstructing the left lower lobe. We

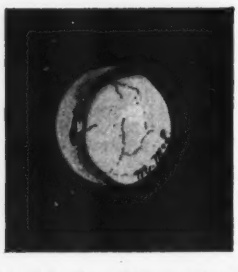

FIGURE 3. *Smooth, Pale, Gray Adenoma Completely Obstructing the Left-Lower-Lobe Bronchus Very Close to the Left-Upper-Lobe Orifice, Which Is Seen at 9 o'clock (Reproduced from Benedict[3] with the Permission of the Publishers).*

treated that bronchoscopically, over fifteen years ago, because the man was about sixty years old and at that time a lobectomy seemed like a good deal of surgery for a benign adenoma. However, that patient had irreparable damage to the lung and after numerous bronchoscopic removals, had to have a lobectomy. We could not find any trace of tumor tissue histologically in the specimen removed, but that is unusual.

This slide (Fig. 4) shows, in contrast to the smooth adenomas, a very irregular gross appearance, characteristic of carcinoma; one can be fooled by a smooth, carcinomatous finger-like projection in the bronchus that may look very much like an adenoma.

DR. SCULLY: Dr. F. Thomas Gephart, who operated on this patient, found it necessary to remove both the right middle and lower lobes because

FIGURE 4. *Fairly Typical Cauliflower Carcinoma of the Right-Lower-Lobe Bronchus Just below the Middle-Lobe Orifice (Reproduced from Benedict,[3] with the Permission of the Publishers).*

the tumor had extended to the margin of the middle-lobe orifice. It arose from the lateral wall of the lower-lobe bronchus and projected slightly into the intermediate bronchus. Microscopically, the tumor was composed of rounded nests of uniform epithelial cells so closely packed as to simulate a diffuse pattern. The lymph nodes recovered from the specimen were free of tumor. The middle lobe was entirely normal both grossly and microscopically. The lower lobe, on the other hand, was completely consolidated by chronic pneumonitis with bronchiectasis, multiple abscesses and organization by fibrosis. Much of the exudate was broken down into cholesterol esters, creating a microscopical picture similar to that of so-called idiopathic cholesterol pneumonitis.

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ON LONGEVITY AS AN IDEAL

LORD HORDER at eighty-two, according to an interview with Morris Fishbein reported in the *Boston Globe*, lays great stress on imperturbability as a prerequisite of longevity. In this he follows Sir William Osler. At the recent meeting of the American Medical Association Dr. Fishbein, when interviewed, announced that he has been seriously practicing imperturbability since adolescence, and also that to live long one should have a sense of humor. Certain "lows," he said, are desirable in order to extend one's days — namely, low blood pressure, low metabolism and low calories. Both the medical and lay press just now bring a mixed bag of guides to long life. Francis Dunbar and Flanders Dunbar reported to the Gerontological Conference at St. Louis, according to the press, a profile of 20 per cent of the more than 1500 white American centenarians. They contend that longevity is not inheritable, that sexual activity is a good thing and quite feasible for the aged, that the strain of child rearing does not shorten life, that the older person's offspring need not love him and finally that one should work hard all his life, however long. They note that people living to a hundred years have above average incomes and education and, happily, almost none of the common illnesses of old age. The incontrovertibility of the statement, in effect, that those who live long are those who live long is to be admired. It is interesting that they are comfortably situated economically, and there is no question that a hundred years of sexual activity softens the sentence of a like amount of hard work.

It is probable that the asthenic person with low blood pressure, windy melancholy and recurrent exhaustion ekes out many years as his metabolism, his weight, his contemporaries and his pleasures fall away. Nevertheless, many of these old persons, even when well off financially and physically, admit that a certain number of years after seventy is enough and that more is a burden. Great age is probably due to a fortuitous, not necessarily a fortunate, combination of circumstances. It may be very human even if not wise to call one's fate good and to make a virtue of necessity. "The prizing of life apart from its content" poses an old, unsettled question. Herodicus, the dietitian and trainer, who indulged in self-treatment was chided by Plato for not curing himself but only putting obstacles in the way of his death until a great age. It may be suspected that some of the unrealistic filial piety publicly professed by middle-aged gerontologists may be a symptom or intimation of their fates should their efforts bring to themselves the still doubtful blessings of advanced age. Too much pother about the aged too often begets only a cackling vanity, a measure of quantitative rather than qualitative values.

As the preparation for the healthy baby starts in fetal life, so the healthful regimen for the aged begins in youth and is as much an affair of the mind and heart as of the body, not one of attaining more

and lower physiologic "lows" as offered by Dr. Fishbein. This is merely the J. Alfred Prufrock method of measuring out one's life with coffee spoons. One is inclined to favor a kind of circumspect extravagance in the use of all the powers God and nature have granted, enhanced as one grows older by whatever reasonable aids nutrition, drugs or endocrines can offer in bolstering up the physical foundations. One does not credit health at the expense of abstemiousness. The best preparation for age is selecting in one's youth the work that gives pleasure and keeping at it as long as one can, limiting it to the proportion that allows the growth and development of nonpersonal interests, remembering that leisure, when not sloth, possibly is more important than work since it may be the indispensable precondition for the religious attitude toward life. Especially interesting in this connection is the finding of the Dunbars that education among the centenarians studied by them was better than average. The top turn and crown of life if truly human is intellectual and spiritual. These functions cannot be imposed on the aged. If acquired in youth and younger adult years, and kept alive by habit and practice, they will not cure but will immeasurably relieve the infirmities of age. As the Hippocratic author of *Visits* says: "Thought is the soul's walk abroad."

WORK FOR ALL WILLING HANDS

ELSEWHERE in this issue of the *Journal* a description will be found of the Cardiac Work Classification Unit about to be opened at the Massachusetts General Hospital under the auspices of various important agencies in the Commonwealth. Although much has been said about the desirability of fitting the partially handicapped person into a suitable place in the economic life of his community, little has so far been done in the matter. Organized work-classification units — obviously not intended to be restricted to cardiac patients — have been operating for only a little over a decade, the first having been opened in New York in 1941, and the second in Cleveland in 1949.

The problems of employability that must be overcome by these efforts are further magnified by the servile obedience of those labor-saving devices that have gone so far to replace manpower in industry, and by a growing population of elderly persons who must be fed and clothed and sheltered regardless of the economic contribution that they are encouraged or permitted to make.

From a purely philosophical point of view one may wonder what employment will be found to keep many idle hands out of mischief when a jigger of atomic energy will power a factory for a month. Somehow, the matter of finding work for persons to perform seems a sounder way of reducing some of the world's dislocations than for technocracy to support in idleness countless thousands who have lost an appreciation of the dignity of labor. Whittling to some purpose might save a self-respect that merely whittling will never salvage.

The purposes of the new clinic are not only to screen workers in regard to their personal employability but even more important to carry on "research in the entire field of physical fitness for various types of work in industry" and, implicit in all such actions, to further education on these problems. The private practitioner elsewhere has found this service a helpful adjunct in his practice; the same experience should be the case with the local project about to be opened.

OVER THE TEACUPS

A SLIGHT stirring of the leaves in the teapot, hardly to be classed as the effect of even a very small tempest, has been occasioned on this side of the water by the presidential address at Dublin on July 7, of P. T. O'Farrell, current head of the British Medical Association.

Dr. O'Farrell, a leading Irish cardiologist, is quoted as having said that "about half of the people who consult doctors are suffering from imaginary illnesses, often unwittingly sponsored by physicians themselves." Careless physicians may thus "even make a cardiac cripple out of a patient who is structurally sound."

It must be admitted that such an allegation is at times not without basis, for even today one may encounter patients whose activities may be unnecessarily restricted, not only because of misinter-

pretation of the doctor's statement, but even on the orders of a doctor who had misinterpreted the patient's statement, as well as certain signs. It must be remembered also that a presidential address is not usually a statistical analysis; "about half" permits some leeway on either side of the line. It is probably quite true, however, that at least "about half" the patients consulting a physician are without important organic disease. Eager, despite the hot weather then prevailing, to reassure the American public, Boston newsmen hastened to the most prominent sources of medical information available to get the local lowdown on President O'Farrell's pronouncement, and were assured that the conditions apparently so prevalent in Eire never exist here — or hardly ever. So much for this midsummer effort, however languid.

A matter of greater concern is the way in which American headline writers attempt to mold the emotions of their readers to their own perpetually frenzied way of thinking. Thus, Dr. O'Farrell's gentle warning, like the famous "white of an egg beat with a gust of wind" becomes "Doctor Lashes Imaginary Ills." The exact definition of "lash" is left as much to the reader's imagination as are the ills, but that does not concern the headline writers.

A question raised regarding the wisdom of a contemplated action becomes an "attack" in this type of verbal pyrotechnics; even this journal, when it gently suggested that the matter of a state medical school might be given further consideration before action was taken, was reported as having "rudely repudiated" the plan and having said, in effect, "that the whole idea is just stuff and nonsense." Such journalism, of course, is not merely intemperate; it is deliberately misinterpreting the information that it is supposed to be reporting.

A servant girl, owned at this time by Mr. C. M. W. of our village, (Woodville, Va.) is the subject of a precocious development of the female reproductive organs and appearance of the menses.

Boston M. & S. J., *August 25, 1852*

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EASTERN STATES EXHIBITION

In co-operation with the Council of the New England State Medical Societies, the Massachusetts Medical Society is sponsoring an exhibit at the Eastern States Exposition to be held in West Springfield, September 14 to 21. The American Medical Association's Bureau of Investigation exhibit exposing mechanical quackery will be displayed. This exhibit presents everything from a "magic horse collar" claimed to magnetize the iron in the blood, to a radioactive "rejuvenator." Many other weird and humorous fake gadgets are shown. A representative of the Bureau of Investigation will be on hand to demonstrate the various gadgets.

BROCKTON FAIR

The Massachusetts Society for Medical Research, with the help of the Woman's Auxiliary to the Massachusetts Medical Society, is sponsoring an exhibit on the benefits of animal research at the Brockton Fair to be held September 6 to 13.

CORRESPONDENCE

PRIORITY OF SPECIAL REGISTRANTS FOR SELECTIVE SERVICE

To the Editor: The enclosed Operations Bulletin No. 76, entitled "Determination of Order of Priority of Special Registrants," issued from General Hershey's office on July 21, 1952, is submitted for publication since it is believed that its contents will be of interest to the readers of the *Journal*.

AUGUSTUS THORNDIKE, M.D., *Chairman*
Massachusetts Advisory Committee
to the Selective Service System
Boston

1. The purpose of this Operations Bulletin is to furnish information with respect to questions which have arisen regarding the determination of the order of priority of special registrants under the provisions of section 4 (i) (2) of the Universal Military Training and Service Act, as amended.

2. (a) Under section 4 (i) (2) of the Act a special registrant who participated as a student in the Army specialized training program or a similar program administered by the Navy, or was deferred from service during World War II, for the purpose of pursuing a course of instruction leading to education in a medical, dental, or allied specialist category is in the first, second, or fourth order of priority depending upon the amount of active duty he has had in the armed forces or the Public Health Service subsequent to his completion of or release from the program or course of instruction exclusive of any time on active duty spent in postgraduate training. If the special registrant has had less than ninety days of such active duty, he is in the first

order of priority, if he has had ninety days or more but less than twenty-one months of such active duty, he is in the second order of priority, or if he has had twenty-one months or more of such active duty, he is in the fourth order of priority.

(b) A special registrant who did not participate as a student in the Army specialized training program or any similar program administered by the Navy, and was not deferred from service during World War II for the purpose of pursuing a course of instruction leading to education in a medical, dental, or allied specialist category is in the third order of priority if he has had no active service in the Army, the Air Force, the Navy, the Marine Corps, the Coast Guard, or the Public Health Service subsequent to September 16, 1940. If he has had any such active service *at any time* subsequent to September 16, 1940, he is in the fourth order of priority. Such active service includes any type of active service as a commissioned officer or as an enlisted man, and also includes any active service spent in postgraduate training while completing an internship, residency, or fellowship in a medical, dental, or allied specialist category.

3. (a) A special registrant who now has a medical, dental, or veterinary degree and who during World War II either was deferred from service in Class II, or participated as a student in the Army specialized training program or the Navy V-12 program, for the purpose of pursuing a course of instruction leading to his education in a field *other* than medicine, dentistry, veterinary medicine, or a specialist category allied to those fields, is not in the first or second order of priority by reason of such deferment or participation in a training program. A special registrant is not in the first or second order of priority because of such deferment or participation in a training program unless at the time the deferment was granted or during the time he participated in the training program, he was pursuing a course of instruction directly leading to his education as a physician, dentist, or veterinarian, or in a specialist category allied thereto. If at that time he was pursuing a course of instruction leading to his education in any other field, for example, engineering, he is not in the first or second order of priority, although subsequent to his completion of or release from the program or course of instruction, he has completed the education necessary for him to become a physician, dentist, or veterinarian.

(b) A special registrant who at the time of his deferment during World War II, or while participating in a training program administered by the armed forces, was pursuing a course of instruction leading to his education in one medical, dental, or allied specialist category and thereafter completed his education in another such category is in the first or second order of priority by reason of such deferment or participation in a training program, if he subsequently has had less than twenty-one months of appropriate active duty. The term "allied specialist categories" includes, but is not limited to, veterinarians, optometrists, pharmacists, and osteopaths. For example, a special registrant who was deferred or participated in a training program for the purpose of pursuing a course of instruction leading to his education as a pharmacist and subsequently has become a physician, dentist, or veterinarian, is in the first or second order of priority if he has had less than twenty-one months of appropriate active duty.

4. Under section 4 (i) (2) of the Act a special registrant is in either the first or second order of priority, when otherwise eligible therefor, depending upon the amount of active duty he has had in the Army, the Air Force, the Navy, the Marine Corps, the Coast Guard, or the Public Health Service subsequent to his completion of or release from the program or course of instruction exclusive of any time spent in postgraduate training. This active duty is not limited to active duty performed in medical, dental, or allied specialist categories. It includes all types of active duty as a commissioned officer or as an enlisted man except active duty spent in postgraduate training while completing an internship, residency, or fellowship in a medical, dental, or allied specialist category. If a special registrant has had two or more separate periods of such active duty, his total amount of active duty is the sum of the lengths of those separate periods.

5. A special registrant is in the first or second order of priority based upon his deferment during World War II for the purpose of pursuing a course of instruction leading to his education in a medical, dental, or allied specialist category only when some portion of his period of deferment was within the period commencing on December 8, 1941, and ending on March 31, 1947. December 8, 1941, was the date of the declaration of war with Japan and the beginning of World War II. Since March 31, 1947, was the date of expiration of those provisions of the Selective Training and Service Act of 1940, as amended, which authorized induction and deferment, all deferments previously granted terminated on that date by operation of law.

6. In some instances a registrant was deferred in Class II-A(F) under the Selective Training and Service Act of 1940, as amended, for the reason that he was at the time of classification pursuing a course of instruction leading to his education in a medical, dental, or allied specialist category. A special registrant who was so deferred in Class II-A(F) during World War II is in either the first or second order of priority depending upon the amount of active duty he has had in the armed forces or the Public Health Service subsequent to the completion of the course of instruction exclusive of any time on active duty spent in postgraduate training, unless he has had twenty-one months or more of such active duty, in which case he is in the fourth order of priority.

7. For the purposes of section 4 (i) (2) of the Act a "course of instruction leading to education in a medical, dental, or allied specialist category" means a course of instruction terminating upon the receipt by the special registrant of his professional degree and does not include any postgraduate training he subsequently performs while completing an internship, residency, or fellowship in a medical, dental, or allied specialist category. Therefore, a special registrant who received his professional degree without deferment and thereafter during World War II was deferred in Class II for the purpose of completing an internship, residency, or fellowship, is not in the first or second order of priority by reason of such deferment.

8. Under section 1650.40 (b) of the Selective Service Regulations those special registrants who are in the first or third order of priority shall be selected for induction in the order of their dates of birth with the youngest being selected first. Those who are in the second or fourth order of priority shall be selected according to their length of active duty in the Army, the Air Force, the Navy, the Marine Corps, the Coast Guard, and the Public Health Service, counting for those in the second order of priority only such active duty they performed subsequent to their completion of or release from the program or course of instruction in which they participated (exclusive of time on active duty spent in postgraduate training while completing an internship, residency, or fellowship), and counting for those in the fourth order of priority all periods of any type of such active duty they performed subsequent to September 16, 1940, with those having the least number of full months of such active duty being selected first.

LEWIS B. HERSHEY, *Director*

FURTHER OPINION ON A STATE MEDICAL SCHOOL

To the Editor: May I comment upon the letter from Dr. Hurwitz, regarding establishment of a state medical school, which appeared in the July 24 issue of the *Journal?*

If the people of the Commonwealth are to be honestly served, the decision regarding a state medical school in Massachusetts should rest on only one point: whether there are enough qualified young people interested in studying medicine to justify a step that would now, as in 1867, divide emoluments and lower the standards of instruction. Dr. Hurwitz says: "It is, of course, true that many of the applicants are not qualified to study medicine. Yet there should be an adequate number of qualified Massachusetts applicants who have oriented their college training toward medical school to fill a new medical school of 100 per class." This is mere supposition.

There can be difference of opinion about who is qualified, but no opinion is valid that does not rest squarely upon the available facts. There are available facts that, so far as I am aware, have not been investigated by the Commission.

The cases of recently unsuccessful candidates, with identity shielded if necessary, as well as the names of the medical schools that rejected them, are available in large numbers. The scholastic performances of these unsuccessful candidates are recorded; their scores on the Medical College Admission Test are on file; the confidential opinions of their professors and others have been studied by groups of men who have devoted many many hours to such appraisals, and who have also checked the reasons for failure on the part of those who fail in the medical schools after having been admitted. These facts should be studied and reported upon before one is asked to accept a supposititious statement that "there should be an adequate number." Suppose there were *not* 100 qualified young people available each year in Massachusetts?

Again admitting that there can be a difference of opinion, I should like to state mine: there are each year very few qualified applicants in Massachusetts who do not gain admission to medical schools. There is, of course, plenty of heartbreak along the dividing line between those who are and those who are not deemed to be qualified, but that must always be. The attempt to squeeze another hundred candidates out of Massachusetts must lead to what is vastly more damaging than inferior instruction — that is, inferior reception of instruction. I am sure that the medical schools of this nation would be glad to co-operate with the Commission if it were to undertake the study suggested in the preceding paragraph, for I am sure that they agree with Dr. Walter Bloedorn, dean at George Washington University School of Medicine, who recently said, "we do not need a single additional poor doctor."

If, after such a study, it can be shown that there are enough qualified young people interested in studying medicine and willing to face the competition that such study entails, I should be disappointed if this Commission did not re-examine the legal background of the statement that "Massachusetts cannot help private educational institutions." The Constitution should be the servant, not the master of the people; if it cannot be amended to meet the changing needs of society and in the best interests of its people, they have ceased to live in a democracy. Perhaps it would not have to be amended; perhaps Massachusetts need only help the individual students, and let the private educational institutions continue to take care of themselves. The private educational institutions have never hesitated to help the Commonwealth of Massachusetts.

DWIGHT O'HARA, M.D.

Waltham Massachusetts

BOOK REVIEWS

Chronic Disease and Psychological Invalidism: A psychosomatic study. By Jurgen Ruesch, M.D. With a foreword by Karl M. Bowman, M.D., 4°, paper, 191 pp., with 11 illustrations and 43 tables. Berkeley: University of California Press, 1951. $3.50.

First published in 1946 as *Psychosomatic Medicine Monograph No. 9*, this book presents and analyzes data derived from the psychiatric, sociologic and psychologic study of 187 patients who had failed to recover within a reasonable time from some physical disease for which they had received the usual medical treatment. The patients had been referred by their own physicians because it was believed that further improvement could not be obtained with ordinary medical treatment. Dr. Ruesch selected 53 of these patients as suitable for brief psychotherapy and reports that the insight thus gained often led the patient to give up his "invalid reaction" and live with, rather than against, himself.

The author's principal thesis is that although any recovery from physical disease depends upon its nature, the rate of recovery is closely related to the conscious or subconscious intention of the patient to get well. Psychosocial factors that had originally influenced the choice of disease were frequently found to be related also to the problem of recovery. But whereas the psychoneurotic is regarded as a victim of unresolved intrapsychic conflict, the patient with delayed recovery is seen as a person for whom the continued illness represents a way out of certain environmentally determined conflicts. In this series of cases, some kind of situational dilemma had come into sharp focus for each patient at about the same time that he became ill. Whether or not this combination of circumstances led to delayed recovery, however, depended upon the prior existence within the patient of an ambivalent character conflict that usually had its roots in an ambiguous childhood situation. As an example, the author cites the case of a boy whose father had encouraged him to be a two-fisted go-getter while his mother was urging him to be a little gentleman. Delayed recovery, according to Dr. Ruesch, stems from conflicts of this kind and is almost exclusively limited to the lower middle class. His psychotherapy begins with a discussion of the focal conflict revolving around the ambivalent situation, the disease itself or the patient's character. Later phases emphasize the role of childhood events in leading up to the patient's present condition. One need not subscribe uncritically to the author's somewhat controversial theoretical orientation to appreciate the significance of his empirical findings. Medical practitioners without specific psychiatric training should encounter in this short book a great many stimulating (and some rather challenging) new ways of thinking about both diagnosis and treatment.

CHARLES P. FONDA, PH.D.

Textbook of Refraction. By Edwin F. Tait, M.D., Ph.D. 8°, cloth, 418 pp., with 93 illustrations. Philadelphia: W. B. Saunders Company, 1951. $8.00.

This book is rightfully a supplement to textbooks of refraction. It is a result of the painstaking application of the author's wide clinical experience in this field. Optics are largely omitted, and the technics of clinical examination are emphasized.

There are many terms that are not familiar to the average refractionist, as well as some statements with which one is not inclined to agree, but the material is presented clearly and with conviction. A considerable portion of the book is devoted to binocular problems. Much space has been given to the method of history taking as well as to many tests that are normally not described in textbooks of refraction.

There are twenty-eight chapters, twenty-seven of which are accompanied by a bibliography that serves as reference for further study. It is regretted that the author did not devote more space to explanations and workings of such popular tests as the "cross cylinder" and "astigmatic dials."

This book deserves a place in the refractionist's library.

ALBERT E. SLOANE, M.D.

Die Exekution des Typus und andere kulturpsychologische Phänomene. By Prof. Dr. Werner Wagner, Munich. 8°, paper, 136 pp. Stuttgart: Georg Thieme, 1951. Paper DM. 15.60. (Distributed by Grune and Stratton, New York.)

In this monograph the author presents his concept of a field that he refers to as cultural psychology and psychopathology, speculating on the meaning of various cultural outgrowths as characteristic of their times. Social phenomena considered "abnormal" by the author can be explained as outgrowths of special constellations in the "cultural psychology" of the period. For instance, a man may embody the feelings of the cultural groups as a whole and, by responding to these feelings, is able to rise to leadership.

Although a consistent system of cultural psychopathology cannot be delineated, its methods as developed by the psychiatrist may give insight into certain broad aspects of social behavior. These problems, which have been treated up to now by sociologists and anthropologists, need to be taken up by psychiatry for a fuller understanding of human motivation.

Man remains with the ability to decide along which lines he may develop himself although cultural patterns may restrict his activities considerably as well as, at times, carry him along with current trends. On the basis of insight gained by the methods of cultural psychopathology, the author suggests therapeutic methods.

A full understanding and appreciation of this work can only be attained by a person well versed in such fields as anthropology, sociology and political science, as well as psychology and psychiatry. The author obviously has such a background. At times his writing will prove difficult to the average reader. His bibliography is comprehensive and covers only the broader aspects of the fields discussed. This is a work well worth the time needed to digest its contents.

JOHN B. HAYES, M.D.

COLLEGE OF AGRICULTURE AND MECHANICAL ARTS LIBRARY SEP 9 52 MARINE BIOLOGICAL LABORATORY

BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

A Textbook of Clinical Pathology. Edited by Seward E. Miller, M.D., medical director, United States Public Health Service, and chief, Division of Occupational Service, Washington, D. C. Fourth edition. 4°, cloth, 1060 pp., with illustrations. Baltimore: The Williams & Wilkins Company, 1952. $9.00.

This book was first issued in 1938 and since then has gone through four editions and six reprintings, which speaks well for its soundness and popularity. The book is the joint effort of eight specialists and is designed to present in one volume the basic scientific information in its field. The text has been completely rearranged and rewritten. Many of the highly technical procedures have been omitted. Short bibliographies of the pertinent literature are appended to the various chapters. The publishing is well done, and the book should be in collections on the subject.

The Child in Health and Disease: A textbook for students and practitioners of medicine. By Clifford G. Grulee, M.D., Rush Professor of Pediatrics, University of Illinois, attending pediatrician, Presbyterian Hospital, Chicago, and chief editor, *American Journal of Diseases of Children;* and R. Cannon Eley, M.D., assistant clinical professor of pediatrics, Harvard Medical School, and chief of Isolation Service and visiting physician, Infants' and Children's Hospital, Boston. Second edition. 4°, cloth, 1255 pp., with illustrations. Baltimore: The Williams & Wilkins Company, 1952. $15.00.

The first edition of this composite book was published in 1948. This new edition, the work of eighty-seven specialists, has been completely revised and brought up to date. New chapters have been added on adoption, medical supervision of summer camps, cardiovascular surgery and viral hepatitis. Short lists of references are appended to the various chapters and there is a comprehensive index. The book should be in all collections on pediatrics.

Intergovernmental Relations in Public Health. By Laurence Wyatt. 4°, paper, 212 pp. Minneapolis: The University of Minnesota Press, 1951. $3.50. (Intergovernmental Relations in the United States, Research Monograph Number 4.)

The studies made in this monograph are based on observations made in the state of Minnesota. The greater part of the text is devoted to a discussion of the United States Public Health Service, the United States Children's Bureau, their inter-relation and the grants-in-aid program. The remainder of the text is devoted to state and local health departments and interstate and local relations. The book should be in all collections on public health.

Bulletin of the Hospital for Joint Diseases, October, 1951: A volume in tribute to Dr. Henry L. Jaffe. 8°, paper, 527 pp., with illustrations. New York: Hospital for Joint Diseases, 1951. $6.00.

This issue of the hospital bulletin is dedicated to Dr. Henry L. Jaffe, pathologist and director of laboratories of the hospital, on the twenty-fifth anniversary of his affiliation with it. Fifty-six physicians have contributed articles on various bone and joint conditions. There is a biographical sketch by Dr. Samuel Kleinberg. The publishing is excellent and the book well illustrated.

Muir's Textbook of Pathology. Revised by D. F. Cappell, M.D., F.R.F.P.S.G., professor of pathology, University of Glasgow, pathologist to the Western Hospitals Group, Glasgow, and consultant pathologist to the Western Regional Board. Sixth edition. 8°, cloth, 1090 pp., with 636 illustrations. Baltimore: The Williams & Wilkins Company, 1951. $10.00.

The first edition of this British work was published in 1924. The need of a sixth edition speaks well for its soundness and popularity. Dr. Cappell has revised the book to bring it up to date and has limited the contents strictly to pathology, omitting such fields as bacteriology and parasitology. The text is devised for medical undergraduates. There is a good index. The printing was done in Great Britain, and the publishing is excellent.

Health Instruction Yearbook 1951. Compiled by Oliver E. Byrd, Ed.D., M.D., professor of health education and director, Department of Hygiene, Stanford University School of Education. With a foreword by Bernice Moss, M.A., Ed.D., president, American Association of Health, Physical Education, and Recreation, and associate professor of health education, University of Utah. 8°, cloth, 236 pp. Stanford, California: Stanford University Press, 1952. $3.50.

This ninth annual issue of a standard reference book presents abstracts of 260 articles published between July 1, 1950, and June 30, 1951. There is a bibliography of the sources of the articles, as well as indexes of authors and subjects.

Cerebral Mechanisms in Behavior: The Hixon symposium. Edited by Lloyd A. Jeffress, professor of psychology, University of Texas. 8°, cloth, 311 pp. New York: John Wiley & Sons, Incorporated, 1951. $6.50.

The Hixon Fund symposium reported in this volume was held at the California Institute of Technology in September, 1948. Five papers were read and were discussed by eleven authorities. The topics covered the relation of the mind to behavior. There are author and subject indexes and the publishing is excellent. The book should be in collections on experimental psychology and psychiatry.

Infective Hepatitis: Studies in East Anglia during the period 1943–47. By F. O. MacCallum, A. M. McFarlan, J. A. R. Miles, M. R. Pollock and C. Wilson. 8°, paper, 144 pp., with 61 tables. London: His Majesty's Stationery Office, 1951. (Privy Council, Medical Research Council Special Report Series No. 273.) 4s. 6d. net.

This comprehensive study of infectious hepatitis was carried out on a large scale in East Anglia, between May, 1943, and December, 1947, during which period the disease was made reportable; clinical observations were made on about 2000 service personnel between November, 1943, and September, 1945. The report is divided into six main parts: epidemiologic, clinical, biochemical, hematologic, serologic, and transmission experiments. Lists of references are appended to the chapters and a summary concludes the text. The special series issued by the Medical Research Council includes many important monographs.

NOTICES

COMBINED ANESTHESIA TEACHING CONFERENCES AT BOSTON

The Combined Anesthesia Teaching Conferences of Boston will be resumed on September 19. Sessions during 1952-1953 will be held on Friday evenings, from 7 to 9 o'clock, at the Massachusetts Memorial Hospitals in the amphitheater of the Evans Memorial, 65 East Newton Street, eighth floor. Interested physicians are invited to attend.

LIFE INSURANCE MEDICAL RESEARCH FUND RESEARCH FELLOWSHIPS AND GRANTS

Applications for awards available July 1, 1953, will be received by the Life Insurance Medical Research Fund as follows: postdoctoral research fellowships, until October 31, 1952 (preference is given to those who wish to work on cardiovascular function and disease or related fundamental problems, the stipends varying from $3,300 to $4,500); and grants to institutions in aid of research on cardiovascular problems, until November 15, 1952. Support is available for physiologic, biochemical and other basic research on cardiovascular problems, as well as for clinical investigation in this field. Further information and application blanks may be obtained from the Scientific Director, Life Insurance Medical Research Fund, 2 East 103d Street, New York 29, New York.

(Notices concluded on page xiii)